

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
4 October 2001 (04.10.2001)

PCT

(10) International Publication Number  
**WO 01/73032 A2**

(51) International Patent Classification<sup>7</sup>: **C12N 15/12**,  
C07K 14/47, C12N 1/21, 5/10, C07K 16/18, G01N 33/68,  
C07K 19/00, C12N 15/10, A61K 38/17, 31/70, 39/395,  
35/14, C12Q 1/68

09/709,729 9 November 2000 (09.11.2000) US

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(21) International Application Number: PCT/US01/09919

(22) International Filing Date: 27 March 2001 (27.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

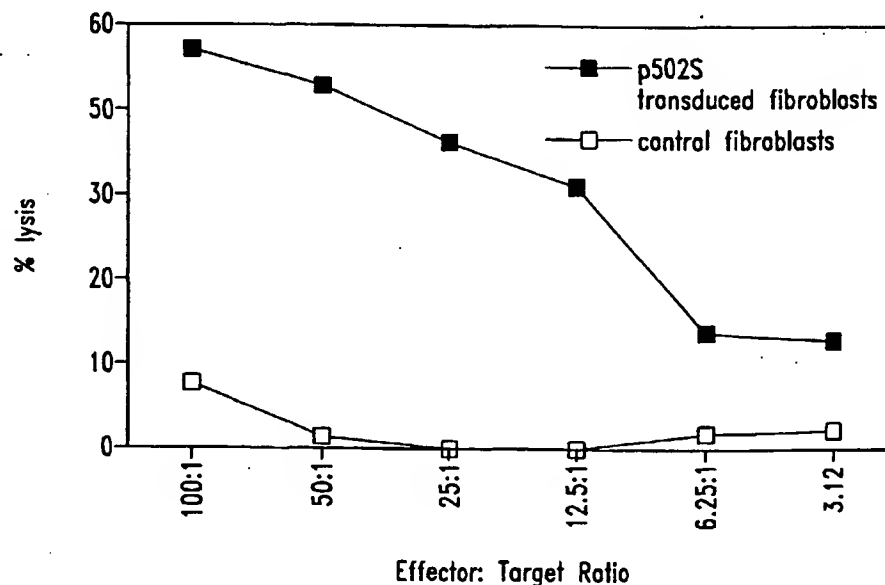
09/536,857	27 March 2000 (27.03.2000)	US
09/568,100	9 May 2000 (09.05.2000)	US
09/570,737	12 May 2000 (12.05.2000)	US
09/593,793	13 June 2000 (13.06.2000)	US
09/605,783	27 June 2000 (27.06.2000)	US
09/636,215	10 August 2000 (10.08.2000)	US
09/651,236	29 August 2000 (29.08.2000)	US
09/657,279	6 September 2000 (06.09.2000)	US
09/679,426	2 October 2000 (02.10.2000)	US
09/685,166	10 October 2000 (10.10.2000)	US

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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly prostate cancer, are disclosed. Illustrative compositions comprise one or more prostate-specific polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly prostate cancer.



WO 01/73032 A2



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(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of  
5 cancer, such as prostate cancer. The invention is more specifically related to  
polypeptides, comprising at least a portion of a prostate-specific protein, and to  
polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides  
are useful in pharmaceutical compositions, *e.g.*, vaccines, and other compositions for  
the diagnosis and treatment of prostate cancer.

### 10 BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although  
Cancer is a significant health problem throughout the world. Although advances have  
been made in detection and therapy of cancer, no vaccine or other universally successful  
method for prevention or treatment is currently available. Current therapies, which are  
15 generally based on a combination of chemotherapy or surgery and radiation, continue to  
prove inadequate in many patients.

Prostate cancer is the most common form of cancer among males, with  
an estimated incidence of 30% in men over the age of 50. Overwhelming clinical  
evidence shows that human prostate cancer has the propensity to metastasize to bone,  
20 and the disease appears to progress inevitably from androgen dependent to androgen  
refractory status, leading to increased patient mortality. This prevalent disease is  
currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate  
cancer remains difficult to treat. Commonly, treatment is based on surgery and/or  
25 radiation therapy, but these methods are ineffective in a significant percentage of cases.  
Two previously identified prostate specific proteins - prostate specific antigen (PSA)  
and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic  
potential. For example, PSA levels do not always correlate well with the presence of

prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other  
5 cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

#### SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide  
10 compositions comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and  
15 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-  
20 931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;  
25

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-



606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-  
5 375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-  
10 375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381,  
15 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%,  
20 and most preferably in at least about 50% of prostate tissue samples tested, at a level that is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for other normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide  
25 sequence described above.

The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383,  
477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586,  
30 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855,

858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858 or 860-862, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant, together with a physiologically acceptable carrier.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

5           Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

10           Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides  
15           encoding such fusion proteins, typically in the form of pharmaceutical compositions, e.g., vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise one or more polypeptide segments for facilitating and/or enhancing the expression,  
20           purification and/or immunogenicity of the polypeptide(s).

Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The patient may be afflicted with prostate cancer, in which case the methods provide  
25           treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition as recited above. The patient may be afflicted

with prostate cancer, in which case the methods provide treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological  
5 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the polypeptide from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological  
10 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a  
polynucleotide encoding such a polypeptide; and (iii) an antigen presenting cell that  
15 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a  
20 patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup>  
and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide  
comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a  
25 polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for  
30 determining the presence or absence of a cancer, preferably a prostate cancer, in a

patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide of the present invention, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to an inventive polynucleotide, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample

obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

## 15 BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

5                Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

              Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell  
10    line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

15                Figure 7 is a Western blot showing the expression of P501S in baculovirus.

              Figure 8 illustrates the results of epitope mapping studies on P501S.

              Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular  
20    domains.

              Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

              Figure 11 shows the results of an ELISA assay to determine the  
25    specificity of rabbit polyclonal antisera raised against P501S.

              Figures 12A(1), 12A(2), 12A(3), and B are the full-length cDNA (SEQ ID NO:777) and predicted amino acid (SEQ ID NO:778) sequences, respectively, for the clone P788P.

              SEQ ID NO: 1 is the determined cDNA sequence for F1-13

30                SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12  
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16  
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1  
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9  
5 SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4  
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17  
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17  
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12  
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12  
10 SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862  
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862  
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13  
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13  
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19  
15 SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19  
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25  
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25  
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24  
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24  
20 SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58  
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58  
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63  
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63  
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4  
25 SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4  
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14  
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14  
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12  
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16  
30 SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21



SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48  
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55  
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2  
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6  
5 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858  
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860  
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861  
SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864  
SEQ ID NO: 41 is the determined cDNA sequence for P5  
10 SEQ ID NO: 42 is the determined cDNA sequence for P8  
SEQ ID NO: 43 is the determined cDNA sequence for P9  
SEQ ID NO: 44 is the determined cDNA sequence for P18  
SEQ ID NO: 45 is the determined cDNA sequence for P20  
SEQ ID NO: 46 is the determined cDNA sequence for P29  
15 SEQ ID NO: 47 is the determined cDNA sequence for P30  
SEQ ID NO: 48 is the determined cDNA sequence for P34  
SEQ ID NO: 49 is the determined cDNA sequence for P36  
SEQ ID NO: 50 is the determined cDNA sequence for P38  
SEQ ID NO: 51 is the determined cDNA sequence for P39  
20 SEQ ID NO: 52 is the determined cDNA sequence for P42  
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25 SEQ ID NO: 57 is the determined cDNA sequence for P55  
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SEQ ID NO: 59 is the determined cDNA sequence for P64  
SEQ ID NO: 60 is the determined cDNA sequence for P65  
SEQ ID NO: 61 is the determined cDNA sequence for P73  
30 SEQ ID NO: 62 is the determined cDNA sequence for P75

SEQ ID NO: 63 is the determined cDNA sequence for P76

SEQ ID NO: 64 is the determined cDNA sequence for P79

SEQ ID NO: 65 is the determined cDNA sequence for P84

SEQ ID NO: 66 is the determined cDNA sequence for P68

5 SEQ ID NO: 67 is the determined cDNA sequence for P80 (also referred  
to as P704P)

SEQ ID NO: 68 is the determined cDNA sequence for P82

SEQ ID NO: 69 is the determined cDNA sequence for U1-3064

SEQ ID NO: 70 is the determined cDNA sequence for U1-3065

10 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692

SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905

SEQ ID NO: 73 is the determined cDNA sequence for V1-3686

SEQ ID NO: 74 is the determined cDNA sequence for R1-2330

SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976

15 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736

SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738

SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741

SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744

20 SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734

SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774

SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781

SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785

SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787

25 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796

SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807

SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810

SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811

SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876

30 SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

- SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896  
SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761  
SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762  
SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766  
5 SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770  
SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771  
SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772  
SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297  
SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309  
10 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278  
SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288  
SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283  
SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304  
SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296  
15 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280  
SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12  
(also referred to as P504S)  
SEQ ID NO: 108 is the predicted amino acid sequence for F1-12  
SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17  
20 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12  
(also referred to as P501S)  
SEQ ID NO: 111 is the determined full length cDNA sequence for N1-  
1862 (also referred to as P503S)  
SEQ ID NO: 112 is the predicted amino acid sequence for J1-17  
25 SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also  
referred to as P501S)  
SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also  
referred to as P503S)  
SEQ ID NO: 115 is the determined cDNA sequence for P89  
30 SEQ ID NO: 116 is the determined cDNA sequence for P90

SEQ ID NO: 117 is the determined cDNA sequence for P92  
SEQ ID NO: 118 is the determined cDNA sequence for P95  
SEQ ID NO: 119 is the determined cDNA sequence for P98  
SEQ ID NO: 120 is the determined cDNA sequence for P102  
5 SEQ ID NO: 121 is the determined cDNA sequence for P110  
SEQ ID NO: 122 is the determined cDNA sequence for P111  
SEQ ID NO: 123 is the determined cDNA sequence for P114  
SEQ ID NO: 124 is the determined cDNA sequence for P115  
SEQ ID NO: 125 is the determined cDNA sequence for P116  
10 SEQ ID NO: 126 is the determined cDNA sequence for P124  
SEQ ID NO: 127 is the determined cDNA sequence for P126  
SEQ ID NO: 128 is the determined cDNA sequence for P130  
SEQ ID NO: 129 is the determined cDNA sequence for P133  
SEQ ID NO: 130 is the determined cDNA sequence for P138  
15 SEQ ID NO: 131 is the determined cDNA sequence for P143  
SEQ ID NO: 132 is the determined cDNA sequence for P151  
SEQ ID NO: 133 is the determined cDNA sequence for P156  
SEQ ID NO: 134 is the determined cDNA sequence for P157  
SEQ ID NO: 135 is the determined cDNA sequence for P166  
20 SEQ ID NO: 136 is the determined cDNA sequence for P176  
SEQ ID NO: 137 is the determined cDNA sequence for P178  
SEQ ID NO: 138 is the determined cDNA sequence for P179  
SEQ ID NO: 139 is the determined cDNA sequence for P185  
SEQ ID NO: 140 is the determined cDNA sequence for P192  
25 SEQ ID NO: 141 is the determined cDNA sequence for P201  
SEQ ID NO: 142 is the determined cDNA sequence for P204  
SEQ ID NO: 143 is the determined cDNA sequence for P208  
SEQ ID NO: 144 is the determined cDNA sequence for P211  
SEQ ID NO: 145 is the determined cDNA sequence for P213  
30 SEQ ID NO: 146 is the determined cDNA sequence for P219

SEQ ID NO: 147 is the determined cDNA sequence for P237  
SEQ ID NO: 148 is the determined cDNA sequence for P239  
SEQ ID NO: 149 is the determined cDNA sequence for P248  
SEQ ID NO: 150 is the determined cDNA sequence for P251  
5 SEQ ID NO: 151 is the determined cDNA sequence for P255  
SEQ ID NO: 152 is the determined cDNA sequence for P256  
SEQ ID NO: 153 is the determined cDNA sequence for P259  
SEQ ID NO: 154 is the determined cDNA sequence for P260  
SEQ ID NO: 155 is the determined cDNA sequence for P263  
10 SEQ ID NO: 156 is the determined cDNA sequence for P264  
SEQ ID NO: 157 is the determined cDNA sequence for P266  
SEQ ID NO: 158 is the determined cDNA sequence for P270  
SEQ ID NO: 159 is the determined cDNA sequence for P272  
SEQ ID NO: 160 is the determined cDNA sequence for P278  
15 SEQ ID NO: 161 is the determined cDNA sequence for P105  
SEQ ID NO: 162 is the determined cDNA sequence for P107  
SEQ ID NO: 163 is the determined cDNA sequence for P137  
SEQ ID NO: 164 is the determined cDNA sequence for P194  
SEQ ID NO: 165 is the determined cDNA sequence for P195  
20 SEQ ID NO: 166 is the determined cDNA sequence for P196  
SEQ ID NO: 167 is the determined cDNA sequence for P220  
SEQ ID NO: 168 is the determined cDNA sequence for P234  
SEQ ID NO: 169 is the determined cDNA sequence for P235  
SEQ ID NO: 170 is the determined cDNA sequence for P243  
25 SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1  
SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1  
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2  
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6  
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13  
30 SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13

SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14

SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14

SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-

4736

5

SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-

4738

SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-

4741

SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-

10 4744

SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-

4774

SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-

4781

15

SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-

4785

SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-

4787

SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-

20 4796

SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-

4807

SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810

SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811

25

SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-

4876

SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-

4884

SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-

30 4896

SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-  
4761

SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-  
4762

5 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-  
4766

SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770  
SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771  
SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-  
10 4772

SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-  
4309

SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-  
4278

15 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-  
4288

SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-  
4283

SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-  
20 4304

SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-  
4296

SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-  
4280

25 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd  
SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con  
SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev  
SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd  
SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev  
30 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

5 SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev  
SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd  
SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev  
SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd  
SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev  
SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd  
SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev  
SEQ ID NO: 220 is the determined cDNA sequence for 8-h11 rev  
SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd  
10 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev  
SEQ ID NO: 223 is the determined cDNA sequence for P509S  
SEQ ID NO: 224 is the determined cDNA sequence for P510S  
SEQ ID NO: 225 is the determined cDNA sequence for P703DE5  
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11  
15 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6  
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7  
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13  
SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
20 SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
25 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
30 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42



SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
5 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
10 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
15 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3  
20 SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
25 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
30 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
5 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
10 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
15 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
20 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8  
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
25 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
30 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

- SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
5 SEQ ID NO: 307 is the determined cDNA sequence for P711P  
SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
10 SEQ ID NO: 312 is the determined cDNA sequence for P715P  
SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously  
15 isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
20 SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
SEQ ID NO: 332 is the determined full length cDNA sequence for  
P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P  
25 (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P  
SEQ ID NO: 335 is the determined cDNA sequence for P705P (also  
referred to as 9-F3)  
SEQ ID NO: 336 is the predicted amino acid sequence for P705P  
30 SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- 5 SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- 10 SEQ ID NO: 345 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens mRNA for E-cadherin
- SEQ ID NO: 346 is the determined cDNA sequence for a clone showing  
homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase  
(SHMT)
- 15 SEQ ID NO: 347 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens natural resistance-associated macrophage protein2  
(NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)
- 20 SEQ ID NO: 349 is the determined cDNA sequence for a clone showing  
homology to Human mRNA for proteasome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- SEQ ID NO: 352 is the determined cDNA sequence for P790P
- 25 SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- SEQ ID NO: 357 is the determined cDNA sequence for P745S
- 30 SEQ ID NO: 358 is the determined cDNA sequence for P782P

- SEQ ID NO: 359 is the determined cDNA sequence for P783P  
SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984  
SEQ ID NO: 361 is the determined cDNA sequence for P787P  
SEQ ID NO: 362 is the determined cDNA sequence for P788P  
5 SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994  
SEQ ID NO: 364 is the determined cDNA sequence for P781P  
SEQ ID NO: 365 is the determined cDNA sequence for P785P  
SEQ ID NO: 366-375 are the determined cDNA sequences for splice  
variants of B305D.
- 10 SEQ ID NO: 376 is the predicted amino acid sequence encoded by the  
sequence of SEQ ID NO: 366.  
SEQ ID NO: 377 is the predicted amino acid sequence encoded by the  
sequence of SEQ ID NO: 372.  
SEQ ID NO: 378 is the predicted amino acid sequence encoded by the  
15 sequence of SEQ ID NO: 373.  
SEQ ID NO: 379 is the predicted amino acid sequence encoded by the  
sequence of SEQ ID NO: 374.  
SEQ ID NO: 380 is the predicted amino acid sequence encoded by the  
sequence of SEQ ID NO: 375.
- 20 SEQ ID NO: 381 is the determined cDNA sequence for B716P.  
SEQ ID NO: 382 is the determined full-length cDNA sequence for  
P711P.  
SEQ ID NO: 383 is the predicted amino acid sequence for P711P.  
SEQ ID NO: 384 is the cDNA sequence for P1000C.  
25 SEQ ID NO: 385 is the cDNA sequence for CGI-82.  
SEQ ID NO: 386 is the cDNA sequence for 23320.  
SEQ ID NO: 387 is the cDNA sequence for CGI-69.  
SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.  
SEQ ID NO: 389 is the cDNA sequence for 23379.  
30 SEQ ID NO: 390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

5 SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor

PDEF.

10 SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

15 SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553 (also known as

P1020C).

20 SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

25 SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

30 SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.  
SEQ ID NO:420 is the cDNA sequence for 22581.  
SEQ ID NO:421 is the cDNA sequence for 22582.  
SEQ ID NO:422 is the cDNA sequence for 22583.  
5 SEQ ID NO:423 is the cDNA sequence for 22584.  
SEQ ID NO:424 is the cDNA sequence for 22585.  
SEQ ID NO:425 is the cDNA sequence for 22586.  
SEQ ID NO:426 is the cDNA sequence for 22587.  
SEQ ID NO:427 is the cDNA sequence for 22588.  
10 SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
SEQ ID NO:432 is the cDNA sequence for 22593.  
15 SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
SEQ ID NO:437 is the cDNA sequence for 22848.  
20 SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
SEQ ID NO:442 is the cDNA sequence for 22854.  
25 SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
SEQ ID NO:447 is the cDNA sequence for 23602.  
30 SEQ ID NO:448 is the cDNA sequence for 23605.

- SEQ ID NO:449 is the cDNA sequence for 23606.
- SEQ ID NO:450 is the cDNA sequence for 23612.
- SEQ ID NO:451 is the cDNA sequence for 23614.
- SEQ ID NO:452 is the cDNA sequence for 23618.
- 5      SEQ ID NO:453 is the cDNA sequence for 23622.
- SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
- SEQ ID NO:455 is the cDNA sequence for LIM protein.
- SEQ ID NO:456 is the cDNA sequence for a known gene.
- SEQ ID NO:457 is the cDNA sequence for a known gene.
- 10      SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:459 is the cDNA sequence for 23045.
- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for clone 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- 15      SEQ ID NO:468-471 are cDNA sequences for P710P.
- SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 20      SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- 25      SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 30



SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

5           SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

10           SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

15           SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

20           SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

25           SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

30           SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P.

SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ  
ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

5 SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID  
NO: 366.

10 SEQ ID NO: 531 is the cDNA sequence of the open reading frame of  
SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of  
SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

15 SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ  
ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ  
ID NO: 535.

20 SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ  
ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-551 are epitopes of P501S.

25 SEQ ID NO: 552 is an extended cDNA sequence for P712P.

SEQ ID NO: 553-568 are the amino acid sequences encoded by  
predicted open reading frames within SEQ ID NO: 552.

SEQ ID NO: 569 is an extended cDNA sequence for P776P.

30 SEQ ID NO: 570 is the determined cDNA sequence for a splice variant  
of P776P referred to as contig 6.

SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

5           SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

10           SEQ ID NO: 575 is the amino acid sequence encoded by a predicted ORF of SEQ ID NO: 571.

SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

15           SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

SEQ ID NO: 591 is an extended cDNA sequence for P1020C.

SEQ ID NO: 592 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: P1020C.

20           SEQ ID NO: 593 is a splice variant of P775P referred to as 50748.

SEQ ID NO: 594 is a splice variant of P775P referred to as 50717. SEQ ID NO: 595 is a splice variant of P775P referred to as 45985.

SEQ ID NO: 596 is a splice variant of P775P referred to as 38769.

SEQ ID NO: 597 is a splice variant of P775P referred to as 37922.

25           SEQ ID NO: 598 is a splice variant of P510S referred to as 49274.

SEQ ID NO: 599 is a splice variant of P510S referred to as 39487.

SEQ ID NO: 600 is a splice variant of P504S referred to as 5167.16.

SEQ ID NO: 601 is a splice variant of P504S referred to as 5167.1.

SEQ ID NO: 602 is a splice variant of P504S referred to as 5163.46.

30           SEQ ID NO: 603 is a splice variant of P504S referred to as 5163.42.

SEQ ID NO: 604 is a splice variant of P504S referred to as 5163.34.

SEQ ID NO: 605 is a splice variant of P504S referred to as 5163.17.

SEQ ID NO: 606 is a splice variant of P501S referred to as 10640.

SEQ ID NO: 607-615 are the sequences of PCR primers.

5       SEQ ID NO: 616 is the determined cDNA sequence of a fusion of P703P  
and PSA.

SEQ ID NO: 617 is the amino acid sequence of the fusion of P703P and  
PSA.

10       SEQ ID NO: 618-689 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 690 is the cDNA sequence of the gene DD3.

SEQ ID NO: 691-697 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 698 is an extended cDNA sequence for P714P.

15       SEQ ID NO: 699-701 are the cDNA sequences for splice variants of  
P704P.

SEQ ID NO: 702 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-14.

20       SEQ ID NO: 703 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-12.

SEQ ID NO: 704 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-10.

SEQ ID NO: 705 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-6.

25       SEQ ID NO: 706 is the amino acid sequence encoded by SEQ ID NO:  
705.

SEQ ID NO: 707 is the amino acid sequence encoded by SEQ ID NO:  
702 SEQ ID NO: 708 is a second amino acid sequence encoded by SEQ ID NO: 702.

30       SEQ ID NO: 709-772 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 773 is a first full-length cDNA sequence for prostate-specific transglutaminase gene (also referred to herein as P558S).

SEQ ID NO: 774 is a second full-length cDNA sequence for prostate-specific transglutaminase gene.

5           SEQ ID NO: 775 is the amino acid sequence encoded by the sequence of SEQ ID NO: 773.

SEQ ID NO: 776 is the amino acid sequence encoded by the sequence of SEQ ID NO: 774.

SEQ ID NO: 777 is the full-length cDNA sequence for P788P.

10           SEQ ID NO: 778 is the amino acid sequence encoded by SEQ ID NO: 777.

SEQ ID NO: 779 is the determined cDNA sequence for a polymorphic variant of P788P.

15           SEQ ID NO: 780 is the amino acid sequence encoded by SEQ ID NO: 779.

SEQ ID NO: 781 is the amino acid sequence of peptide 4 from P703P.

SEQ ID NO: 782 is the cDNA sequence that encodes peptide 4 from P703P.

20           SEQ ID NO: 783-798 are the cDNA sequence encoding epitopes of P703P.

SEQ ID NO: 799-814 are the amino acid sequences of epitopes of P703P.

SEQ ID NO: 815 and 816 are PCR primers.

25           SEQ ID NO: 817 is the cDNA sequence encoding an N-terminal portion of P788P expressed in *E. coli*.

SEQ ID NO: 818 is the amino acid sequence of the N-terminal portion of P788P expressed in *E. coli*.

SEQ ID NO: 819 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

30           SEQ ID NO: 820 and 821 are PCR primers.

SEQ ID NO: 822 is the cDNA sequence for the Ra12-P510S-C construct.

SEQ ID NO: 823 is the cDNA sequence for the P510S-C construct.

SEQ ID NO: 824 is the cDNA sequence for the P510S-E3 construct.

5 SEQ ID NO: 825 is the amino acid sequence for the Ra12-P510S-C construct.

SEQ ID NO: 826 is the amino acid sequence for the P510S-C construct.

SEQ ID NO: 827 is the amino acid sequence for the P510S-E3 construct.

SEQ ID NO: 828-833 are PCR primers.

10 SEQ ID NO: 834 is the cDNA sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 835 is the amino acid sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 836 and 837 are PCR primers.

15 SEQ ID NO: 838 is the determined amino acid sequence for a P703P His tag fusion protein.

SEQ ID NO: 839 is the determined cDNA sequence for a P703P His tag fusion protein.

SEQ ID NO: 840 and 841 are PCR primers.

20 SEQ ID NO: 842 is the determined amino acid sequence for a P705P His tag fusion protein.

SEQ ID NO: 843 is the determined cDNA sequence for a P705P His tag fusion protein.

SEQ ID NO: 844 and 845 are PCR primers.

25 SEQ ID NO: 846 is the determined amino acid sequence for a P711P His tag fusion protein.

SEQ ID NO: 847 is the determined cDNA sequence for a P711P His tag fusion protein.

30 SEQ ID NO: 848 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 849 and 850 are PCR primers.

SEQ ID NO: 851 is the determined cDNA sequence for the construct Ra12-P501S-E2.

5 SEQ ID NO: 852 is the determined amino acid sequence for the construct Ra12-P501S-E2.

SEQ ID NO: 853 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 854 is the DNA sequence encoding SEQ ID NO: 853.

SEQ ID NO: 855 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 856 is the DNA sequence encoding SEQ ID NO: 855.

10 SEQ ID NO: 857 is a peptide employed in epitope mapping studies.

SEQ ID NO: 858 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 859 is the DNA sequence encoding SEQ ID NO: 858.

SEQ ID NO: 860-862 are the amino acid sequences for CD4 epitopes of P501S.

15 SEQ ID NO: 863-865 are the DNA sequences encoding the sequences of SEQ ID NO: 860-862.

SEQ ID NO: 866-877 are the amino acid sequences for putative CTL epitopes of P703P.

SEQ ID NO: 878 is the full-length cDNA sequence for P789P.

20 SEQ ID NO: 879 is the amino acid sequence encoded by SEQ ID NO: 878.

SEQ ID NO: 880 is the determined full-length cDNA sequence for the splice variant of P776P referred to as contig 6.

25 SEQ ID NO: 881-882 are determined full-length cDNA sequences for the splice variant of P776P referred to as contig 7.

SEQ ID NO: 883-887 are amino acid sequences encoded by SEQ ID NO: 880.

SEQ ID NO: 888-893 are amino acid sequences encoded by the splice variant of P776P referred to as contig 7.

SEQ ID NO: 894 is the full-length cDNA sequence for human transmembrane protease serine 2.

SEQ ID NO: 895 is the amino acid sequence encoded by SEQ ID NO: 894.

5           SEQ ID NO: 896 is the cDNA sequence encoding the first 209 amino acids of human transmembrane protease serine 2.

SEQ ID NO: 897 is the first 209 amino acids of human transmembrane protease serine 2.

10           SEQ ID NO: 898 is the amino acid sequence of peptide 296-322 of P501S.

SEQ ID NO: 899-902 are PCR primers.

SEQ ID NO: 903 is the determined cDNA sequence of the Vb chain of a T cell receptor for the P501S-specific T cell clone 4E5.

15           SEQ ID NO: 904 is the determined cDNA sequence of the Va chain of a T cell receptor for the P501S-specific T cell clone 4E5.

SEQ ID NO: 905 is the amino acid sequence encoded by SEQ ID NO 903.

SEQ ID NO: 906 is the amino acid sequence encoded by SEQ ID NO 904.

20           SEQ ID NO: 907 is the full-length open reading frame for P768P including stop codon.

SEQ ID NO: 908 is the full-length open reading frame for P768P without stop codon.

25           SEQ ID NO: 909 is the amino acid sequence encoded by SEQ ID NO: 908.

SEQ ID NO: 910-915 are the amino acid sequences for predicted domains of P768P.

SEQ ID NO: 916 is the full-length cDNA sequence of P835P.

30           SEQ ID NO: 917 is the cDNA sequence of the previously identified clone FLJ13581.



SEQ ID NO: 918 is the cDNA sequence of the open reading frame for P835P with stop codon.

SEQ ID NO: 919 is the cDNA sequence of the open reading frame for P835P without stop codon.

5 SEQ ID NO: 920 is the full-length amino acid sequence for P835P.

SEQ ID NO: 921-928 are the amino acid sequences of extracellular and intracellular domains of P835P.

SEQ ID NO: 929 is the full-length cDNA sequence for P1000C.

10 SEQ ID NO: 930 is the cDNA sequence of the open reading frame for P1000C, including stop codon.

SEQ ID NO: 931 is the cDNA sequence of the open reading frame for P1000C, without stop codon.

SEQ ID NO: 932 is the full-length amino acid sequence for P1000C.

SEQ ID NO: 933 is amino acids 1-100 of SEQ ID NO: 932.

15 SEQ ID NO: 934 is amino acids 100-492 of SEQ ID NO: 932.

SEQ ID NO: 935-937 are PCR primers.

SEQ ID NO: 938 is the cDNA sequence of the expressed full-length P767P coding region.

20 SEQ ID NO: 939 is the cDNA sequence of an expressed truncated P767P coding region.

SEQ ID NO: 940 is the amino acid sequence encoded by SEQ ID NO: 939.

SEQ ID NO: 941 is the amino acid sequence encoded by SEQ ID NO: 938.

25 SEQ ID NO: 942 is the DNA sequence of a CD4 epitope of P703P.

SEQ ID NO: 943 is the amino acid sequence of a CD4 epitope of P703P.

## DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly prostate cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (*e.g.*, T cells).

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); Maniatis et al. *Molecular Cloning: A Laboratory Manual* (1982); *DNA Cloning: A Practical Approach*, vol. I & II (D. Glover, ed.); *Oligonucleotide Synthesis* (N. Gait, ed., 1984); *Nucleic Acid Hybridization* (B. Hames & S. Higgins, eds., 1985); *Transcription and Translation* (B. Hames & S. Higgins, eds., 1984); *Animal Cell Culture* (R. Freshney, ed., 1986); Perbal, *A Practical Guide to Molecular Cloning* (1984).

All publications, patents and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

Polypeptide Compositions

As used herein, the term "polypeptide" is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-

expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of  
5 this invention are amino acid subsequences comprising epitopes, i.e., antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111,  
10 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide  
15 sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In specific embodiments, the polypeptides of the invention comprise amino acid sequences as set  
20 forth in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

25 The polypeptides of the present invention are sometimes herein referred to as prostate-specific proteins or prostate-specific polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in prostate tissue samples. Thus, a "prostate-specific polypeptide" or "prostate-specific protein," refers generally to a polypeptide sequence of the present  
30 invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed

in a substantial proportion of prostate tissue samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of prostate tissue samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in other  
5 normal tissues, as determined using a representative assay provided herein. A prostate-specific polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

In certain preferred embodiments, the polypeptides of the invention are  
10 immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with prostate cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, *Antibodies: A Laboratory*  
15 *Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

20 As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide.  
25 Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they  
30 specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other

immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that  
5 is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that  
10 have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain  
15 has been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells  
20 and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies  
25 that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide composition set forth herein, such as those set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-  
5 380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-  
10 335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally  
15 encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described below), along its length, to a polypeptide sequence set forth herein.

In one preferred embodiment, the polypeptide fragments and variants  
20 provided by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set forth herein.

In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or  
25 more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally  
30 occurring or may be synthetically generated, for example, by modifying one or more of

the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader  
5 sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another  
10 amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide  
15 with desirable characteristics, *e.g.*, with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

20 For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence  
25 substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids			Codons						
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

In making such changes, the hydrophatic index of amino acids may be considered. The importance of the hydrophatic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydrophatic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydrophatic index on the basis of its



hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5);  
5 glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are  
10 within  $\pm 2$  is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of  
15 its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0  $\pm$  1); glutamate (+3.0  $\pm$  1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (-0.4); proline (-0.5  $\pm$  1); alanine (-0.5); histidine (-0.5); cysteine  
20 (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5); tryptophan (-3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within  $\pm 2$   
25 is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that  
30 take various of the foregoing characteristics into consideration are well known to those

of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of  
5 flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

10 Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values  
15 include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a  
20 preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

25 As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For  
30 example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be "identical" if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

- Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

- Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics

Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known

tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al.,

*Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to  
5 separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and  
10 transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus,  
15 tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression  
20 and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent  
25 and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; *see also, Skeiky et al., Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the  
30 purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous

immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least  
5 about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions,  
10 additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a  
15 portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino  
20 acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells.  
25 Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is  
30 derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine

amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been  
5 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at  
10 residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention,  
15 when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4<sup>+</sup> T-cells specific for the polypeptide.

Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further  
20 described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a  
25 growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of  
30 the invention are isolated. An "isolated" polypeptide is one that is removed from its



original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, *e.g.*, are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure.

#### Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably an immunogenic variant or derivative, of such a sequence.

5           Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823,  
10 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-  
15 931, 938, 939 and 942, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In certain preferred  
20 embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

          In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-  
25 335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this  
30 invention using the methods described herein, (*e.g.*, BLAST analysis using standard

parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

5 Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous  
10 genes of xenogenic origin.

In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to, or complementary to, one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at  
15 least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103,  
20 *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary  
25 sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for  
30 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in

the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions,

usually 30 to about 75, preferably 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using  
5 the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical  
10 Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-  
15 425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI),  
25 or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST  
30 2.0 can be used, for example with the parameters described herein, to determine percent

sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always  $>0$ ) and N (penalty score for mismatching residues; always  $<0$ ). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present

invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25

nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.



As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable  
5 signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known  
10 rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

15 In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

20 In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 contiguous nucleotides that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence  
25 disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a  
30 sequence of interest will enable them to be of use in detecting the presence of

complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of  
5 contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in  
10 various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger  
15 contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in  
20 length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

25 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various

factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, e.g., one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to

destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention,  
5 polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis  
10 is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1,  
15 striatal GABA<sub>A</sub> receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a  
20 variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a  
25 complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In  
30 each case, preferred compositions comprise a sequence region that is complementary,

and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure,  $T_m$ ,  
5 binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary  
10 to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997 Sep 1;25(17):3389-402).

The use of an antisense delivery method employing a short peptide  
15 vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered  
20 into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme  
25 molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For  
30 example, a large number of ribozymes accelerate phosphoester transfer reactions with a

high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement  
5 that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general,  
10 enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to  
15 cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many  
20 technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of  
25 target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action  
30 (Woolf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the

specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis  $\delta$  virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis  $\delta$  virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada *et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO

92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes



expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number of methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem.* 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*,

Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will  
5 depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed  
10 by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that  
15 contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and  
20 utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*, Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*,  
25 Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to  
30 therapeutics.

Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

#### Polynucleotide Identification, Characterization and Expression

Polynucleotide compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena *et al.*, *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller *et al.*, *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by

reference in its entirety. Briefly, in PCR™, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present  
5 in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse  
10 transcription and PCR™ amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR™ amplification technique, are readily known and available in  
15 the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat.  
20 Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded  
25 RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara,  
30 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (e.g., a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification.

- 5 Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

- For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or  
10 bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may  
15 be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can  
20 then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

- Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.*  
25 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a  
30 known region. The amplified sequences are typically subjected to a second round of

amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or  
5 RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed  
10 to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs  
15 may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct  
20 expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous  
25 in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring  
30 sequence.

Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be

confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

5           In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, *i.e.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing  
10 sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et  
15 al. (1989) Current Protocols in Molecular Biology, John Wiley & Sons, New York. N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid,  
20 or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

25           The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription  
30 and translation elements, including constitutive and inducible promoters, may be used.



For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example, when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of .beta.-galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For

example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91:3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which

successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of

skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

5                   A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal  
10 antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; Serological Methods, a Laboratory Manual, APS Press, St Paul, Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

15                   A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions  
20 thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used  
25 include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained  
30 intracellularly depending on the sequence and/or the vector used. As will be understood

by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant  
5 or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

10 Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant ( $K_d$ ) of the interaction, wherein a smaller  $K_d$  represents a greater  
15 affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both  
20 the "on rate constant" ( $K_{on}$ ) and the "off rate constant" ( $K_{off}$ ) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of  $K_{off}/K_{on}$  enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant  $K_d$ . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

25 An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable  
30 regions" which are interposed between more conserved flanking stretches known as

"framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation



of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab)<sub>2</sub>" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V<sub>H</sub>::V<sub>L</sub> heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V<sub>H</sub>::V<sub>L</sub> heterodimer which is expressed from a gene fusion including V<sub>H</sub>- and V<sub>L</sub>-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an

antigen-binding site. See, *e.g.*, U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRS and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (*e.g.*, a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRS. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) Nature 349:293-299; Lobuglio et al. (1989) Proc. Nat. Acad. Sci. USA 86:4220-4224; Shaw et al. (1987) J Immunol. 138:4534-4538; and Brown et al. (1987) Cancer Res. 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) Nature 332:323-327; Verhoeyen et al. (1988) Science 239:1534-1536; and Jones et al. (1986) Nature 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, *e.g.*, a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) Ann. Rev. Biochem. 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (*e.g.*, solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (*e.g.*, electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in

this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred  
5 toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a  
10 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an  
15 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which  
20 otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,  
25 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of  
30 different cleavable linker groups have been described. The mechanisms for the

intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by  
5 serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody.  
10 Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent  
15 bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for  
20 radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For  
25 example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

### T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells

may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et



al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

#### Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, e.g., other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as

described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (e.g., salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve

the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian  
5 host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered  
10 to a subject. A number of illustrative retroviral systems have been described (*e.g.*, U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

15 In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using  
25 techniques well known in the art. See, *e.g.*, U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines* 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-539; Muzyczka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129;

Kotin, R. M. (1994) *Human Gene Therapy* 5:793-801; Shelling and Smith (1994) *Gene Therapy* 1:165-169; and Zhou et al. (1994) *J. Exp. Med.* 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK<sup>sup</sup>(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected in vitro with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, e.g., Elroy-Stein and Moss, *Proc. Natl. Acad. Sci. USA* (1990) 87:6743-6747; Fuerst et al. *Proc. Natl. Acad. Sci. USA* (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer

protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant  
5 Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, *e.g.*, WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in  
10 U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery  
15 under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487;  
20 WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al.,  
25 *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in a specific location and orientation via homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the  
30 polynucleotide may be stably maintained in the cell as a separate, episomal segment of

DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression  
5 construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable  
10 beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK)  
15 and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device,  
20 propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639  
25 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances  
30 or potentiates an immune response (antibody and/or cell-mediated) to an exogenous

antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins.

- 5 Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated  
10 sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

- Within certain embodiments of the invention, the adjuvant composition  
15 is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as  
20 provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman,  
25 *Ann. Rev. Immunol.* 7:145-173, 1989.

- Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL® adjuvants are available from Corixa Corporation (Seattle, WA; *see*, for example, US  
30 Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing

oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by

5 Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example

10 combinations of at least two of the following group comprising QS21, QS7, Quil A,  $\beta$ -escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix,

15 particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or

20 suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol<sup>R</sup> to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

In one preferred embodiment, the adjuvant system includes the

25 combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL<sup>®</sup> adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-

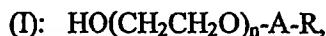


MPL<sup>®</sup> adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of  
5 CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series  
10 of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn<sup>®</sup>; Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene  
15 ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



wherein,  $n$  is 1-50,  $A$  is a bond or  $-\text{C}(\text{O})-$ ,  $R$  is  $\text{C}_{1-50}$  alkyl or Phenyl  $\text{C}_{1-50}$  alkyl.

20 One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein  $n$  is between 1 and 50, preferably 4-24, most preferably 9; the  $R$  component is  $\text{C}_{1-50}$ , preferably  $\text{C}_4\text{-C}_{20}$  alkyl and most preferably  $\text{C}_{12}$  alkyl, and  $A$  is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably  
25 from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck  
30 index (12<sup>th</sup> edition: entry 7717). These adjuvant molecules are described in WO

99/52549. The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

5                   According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or  
10 maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

15                   Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In  
20 general, dendritic cells may be identified based on their typical shape (*stellate in situ*, with marked cytoplasmic processes (*dendrites*) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex*  
25 *vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

                  Dendritic cells and progenitors may be obtained from peripheral blood,  
30 bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph

nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from  
5 peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature"  
10 cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature  
15 phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the  
20 invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be  
25 administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or  
30 progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or

RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated  
5 immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration,  
10 including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release.  
15 In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers  
20 include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends  
25 upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (*e.g.*, polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S.  
30 Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763;

5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they

may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 5 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, 10 cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to 15 materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds 20 may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of 25 active compound(s) in each therapeutically useful composition may be prepared is such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a 30 variety of dosages and treatment regimens may be desirable.

For oral administration, the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

10 In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

20 Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or

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by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride.

5 Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered

10 isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml

15 of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity

20 standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for

25 example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be



administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption  
5 delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase  
10 "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the  
15 lungs via nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of  
20 a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid  
25 particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example,  
30 Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998

Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

5               Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery  
10 systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

15               In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

                  Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the  
20 present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1  $\mu$ m) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for  
25 example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of prostate cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The

polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g., intracutaneous,*

intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies)

obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the  
5 biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in  
10 the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c)  
15 comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding  
20 agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized  
25 binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and polypeptide portions thereof to which the binding agent binds, as  
30 described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized

on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a  
5 different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically  
10 blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact  
15 time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve  
20 equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second  
25 antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of  
30 binding that occurs over a period of time. Unbound detection reagent is then removed



and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

10 To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with  
15 samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985,  
20 p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a  
25 signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10

nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the  
5 diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold*  
10 *Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules.  
15 PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold  
20 or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above  
25 for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the

cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound  
5 binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific  
10 for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

15 The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein.  
20 Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

25 Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be

present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

## EXAMPLE 1

## 5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from  
10 prostate tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA  
15 was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns  
20 (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA  
25 libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$  independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones  
30 having inserts and the average insert size being 1120 base pairs. For both libraries,

sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor  
5 and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol  
10 precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the  
15 DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of  
20 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three  
25 more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E.*



*coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12 (also referred to as P504S). This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108. cDNA splice variants of P504S are provided in SEQ ID NO: 600-605.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1  $\mu$ g each of human glandular kallikrein, PSA and

mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

5 Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA  
10 sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively).  
15 Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike,  
20 four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant  
25 homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding

predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S. A cDNA splice variant of P501S is provided in SEQ ID NO: 606.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807,

1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the  
5 isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were  
10 over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-  
15 4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively,  
20 and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297,  
25 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-4278, 1D-4288, 1D-

4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively. Additional splice variants of P510S are provided in SEQ ID NO: 598 and 599.

The determined cDNA sequences for additional prostate-specific clones isolated during characterization of prostate specific cDNA libraries are provided in SEQ ID NO: 618-689, 691-697 and 709-772. Comparison of these sequences with those in the public databases revealed no significant homologies to any of these sequences.

## EXAMPLE 2

## DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

5           Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

10           Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was  
15           used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for  
20           each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

          mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung  
25           tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at  
30           high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon

and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at  
5 low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

10 Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also  
15 expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal  
20 muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and  
25 kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow,  
30 brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney,

ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. Subsequent comparison of the sequence of SEQ ID NO: 384 with sequences in the public databases, led to the identification of a full-length cDNA sequence of P1000C (SEQ ID NO: 929), which encodes a 492 amino acid sequence.



Analysis of the amino acid sequence using the PSORT II program led to the identification of a putative transmembrane domain from amino acids 84-100. The cDNA sequence of the open reading frame of P1000C, including the stop codon, is provided in SEQ ID NO: 930, with the open reading frame without the stop codon being  
5 provided in SEQ ID NO: 931. The full-length amino acid sequence of P1000C is provided in SEQ ID NO: 932. SEQ ID NO: 933 and 934 represent amino acids 1-100 and 100-492 of P1000C, respectively.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by  
10 immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

15 The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver,  
20 brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that  
25 this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

## EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC  
POLYPEPTIDES BY PCR-BASED SUBTRACTION

5           A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The  
10 resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

          Fifty-nine positive clones were sequenced. Comparison of the DNA  
15 sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID  
20 NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

          Further studies employing the sequence of SEQ ID NO: 67 as a probe in standard full-length cloning methods, resulted in the isolation of three cDNA sequences  
25 which appear to be splice variants of P80 (also known as P704P). These sequences are provided in SEQ ID NO: 699-701.

          Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA  
30 sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145,

147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones  
5 containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is  
10 provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine  
15 and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed  
20 comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor  
25 compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal  
30 prostate and prostate tumor, compared to six of twelve other normal tissues tested.

Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and  
5 normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-  
10 h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in  
15 the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

20 mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor  
25 and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those  
5 in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

10 PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in  
15 SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of  
20 the putative signal sequence. The full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding amino acid sequence being provided in SEQ ID NO: 525.

Using computer algorithms, the following regions of P703P were predicted to represent potential HLA A2-binding CTL epitopes: amino acids 164-172  
25 of SEQ ID NO: 525 (SEQ ID NO: 866); amino acids 160-168 of SEQ ID NO: 525 (SEQ ID NO: 867); amino acids 239-247 of SEQ ID NO: 525 (SEQ ID NO: 868); amino acids 118-126 of SEQ ID NO: 525 (SEQ ID NO: 869); amino acids 112-120 of SEQ ID NO: 525 (SEQ ID NO: 870); amino acids 155-164 of SEQ ID NO: 525 (SEQ ID NO: 871); amino acids 117-126 of SEQ ID NO: 525 (SEQ ID NO: 872); amino acids  
30 164-173 of SEQ ID NO: 525 (SEQ ID NO: 873); amino acids 154-163 of SEQ ID NO:

525 (SEQ ID NO: 874); amino acids 163-172 of SEQ ID NO: 525 (SEQ ID NO: 875); amino acids 58-66 of SEQ ID NO: 525 (SEQ ID NO: 876); and amino acids 59-67 of SEQ ID NO: 525 (SEQ ID NO: 877).

P703P was found to show some homology to previously identified  
5 proteases, such as thrombin. The thrombin receptor has been shown to be preferentially expressed in highly metastatic breast carcinoma cells and breast carcinoma biopsy samples. Introduction of thrombin receptor antisense cDNA has been shown to inhibit the invasion of metastatic breast carcinoma cells in culture. Antibodies against thrombin receptor inhibit thrombin receptor activation and thrombin-induced platelet  
10 activation. Furthermore, peptides that resemble the receptor's tethered ligand domain inhibit platelet aggregation by thrombin. P703P may play a role in prostate cancer through a protease-activated receptor on the cancer cell or on stromal cells. The potential trypsin-like protease activity of P703P may either activate a protease-activated receptor on the cancer cell membrane to promote tumorigenesis or activate a protease-  
15 activated receptor on the adjacent cells (such as stromal cells) to secrete growth factors and/or proteases (such as matrix metalloproteinases) that could promote tumor angiogenesis, invasion and metastasis. P703P may thus promote tumor progression and/or metastasis through the activation of protease-activated receptor. Polypeptides and antibodies that block the P703P-receptor interaction may therefore be usefully  
20 employed in the treatment of prostate cancer.

To determine whether P703P expression increases with increased severity of Gleason grade, an indicator of tumor stage, quantitative PCR analysis was performed on prostate tumor samples with a range of Gleason scores from 5 to > 8. The mean level of P703P expression increased with increasing Gleason score, indicating that  
25 P703P expression may correlate with increased disease severity.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences  
30 for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are

provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P

were found. Further studies employing the sequence of SEQ ID NO: 334 as a probe in standard full-length cloning methods, resulted in an extended cDNA sequence for P714P. This sequence is provided in SEQ ID NO: 698. This sequence was found to show some homology to the gene that encodes human ribosomal L23A protein.

5 Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

10 Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an  
15 ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483. Additional splice variants of P775P are provided in SEQ ID NO: 593-597.

Subsequent studies led to the identification of a genomic region on  
20 chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led to the identification of a potential  
25 open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

Comparison of the clone of SEQ ID NO: 325 (referred to as P558S) with sequences in the GenBank and GeneSeq DNA databases showed that P558S is identical to the prostate-specific transglutaminase gene, which is known to have two forms. The  
30 full-length sequences for the two forms are provided in SEQ ID NO: 773 and 774, with



the corresponding amino acid sequences being provided in SEQ ID NO: 775 and 776, respectively. The cDNA sequence of SEQ ID NO: 774 has a 15 pair base insert, resulting in a 5 amino acid insert in the corresponding amino acid sequence (SEQ ID NO: 776). This insert is not present in the sequence of SEQ ID NO: 773.

5 Further studies on P768P (SEQ ID NO: 315) led to the identification of the putative full-length open reading frame (ORF). The cDNA sequence of the ORF with stop codon is provided in SEQ ID NO: 907. The cDNA sequence of the ORF without stop codon is provided in SEQ ID NO: 908, with the corresponding amino acid sequence being provided in SEQ ID NO: 909. This sequence was found to show 86%  
10 identity to a rat calcium transporter protein, indicating that P768P may represent a human calcium transporter protein. The locations of transmembrane domains within P768P were predicted using the PSORT II computer algorithm. Six transmembrane domains were predicted at amino acid positions 118-134, 172-188, 211-227, 230-246, 282-298 and 348-364. The amino acid sequences of SEQ ID NO: 910-915 represent  
15 amino acids 1-134, 135-188, 189-227, 228-246, 247-298 and 299-511 of P768P, respectively.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

20

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of  
25 conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid  
30 (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of

0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

5

## EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF  
PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

10 A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide  
15 restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

20 The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate  
25 hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences  
30 which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich  
5 differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

10 In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for  
15 proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA  
20 sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant  
25 homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most  
30 prostate tumors and BPH tissues by a factor of three or greater, with elevated expression

seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

5 Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349,  
10 351, 355-359, 361, 362 and 364, were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant  
15 homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365.

Comparison of the sequence of SEQ ID NO: 362 with sequences in the GenBank and GeneSeq DNA databases showed that this clone (referred to as P788P) is identical to GeneSeq Accession No. X27262, which encodes a protein found in the GeneSeq protein Accession No. Y00931. The full length cDNA sequence of P788P is  
20 shown in Figure 12A (SEQ ID NO: 777), with the corresponding predicted amino acid being shown in Figure 12B (SEQ ID NO: 778). Subsequently, a full-length cDNA sequence for P788P that contains polymorphisms not found in the sequence of SEQ ID NO: 779, was cloned multiple times by PCR amplification from cDNA prepared from several RNA templates from three individuals. This determined cDNA sequence of this  
25 polymorphic variant of P788P is provided in SEQ ID NO: 779, with the corresponding amino acid sequence being provided in SEQ ID NO: 780. The sequence of SEQ ID NO: 780 differs from that of SEQ ID NO: 778 by six amino acid residues. The P788P protein has 7 potential transmembrane domains at the C-terminal portion and is predicted to be a plasma membrane protein with an extracellular N-terminal region.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEQ ID NO: 569. The determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively. Further studies led to the isolation of the full-length sequence for the clone of SEQ ID NO: 570 (provided in SEQ ID NO: 880). Full-length cloning efforts on the clone of SEQ ID NO: 571 led to the isolation of two sequences (provided in SEQ ID NO: 881 and 882), representing a single clone, that are identical with the exception of a polymorphic insertion/deletion at position 1293. Specifically, the clone of SEQ ID NO: 882 (referred to as clone F1) has a C at position 1293. The clone of SEQ ID NO: 881 (referred to as clone F2) has a single base pair deletion at position 1293. The predicted amino acid sequences encoded by 5 open reading frames located within SEQ ID NO: 880 are provided in SEQ ID NO: 883-887, with the predicted amino acid sequences encoded by the clone of SEQ ID NO: 881 and 882 being provided in SEQ ID NO: 888-893.

Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common,

suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

5           The clone of SEQ ID NO: 342 (referred to as P789P) was found to show homology to a previously identified gene. The full length cDNA sequence for P789P and the corresponding amino acid sequence are provided in SEQ ID NO: 878 and 879, respectively.

10

## EXAMPLE 6

## PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

15           Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were  
20 immunized with 100µg of P2S#12 and 120µg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium  
25 pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ( $5 \times 10^5$ /ml) were  
30 restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells

(Sherman et al, *Science* 258:815-818, 1992) and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200  $\mu$ g/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes,

CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

5 Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single  
10 cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells ( $5 \times 10^5$ /ml) were restimulated  
15 with  $2.5 \times 10^6$ /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as  
20 shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were  
25 isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.



## EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION

## WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred  
5 to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research  
Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012  
either intramuscularly or intradermally. The mice were immunized three times, with a  
two week interval between immunizations. Two weeks after the last immunization,  
immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator  
10 cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL  
activity was assessed against P501S transduced targets. Two out of 8 mice developed  
strong anti-P501S CTL responses. These results demonstrate that P501S contains at  
least one naturally processed HLA-A2-restricted CTL epitope.

15

## EXAMPLE 8

## ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate  
tumor polypeptide to recognize human tumor.

20

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ  
ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells  
according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75,  
1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to  
recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which  
25 were transduced to express the P502S gene in a γ-interferon ELISPOT assay (*see*  
Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells  
were assayed in duplicate on 10<sup>4</sup> fibroblasts in the presence of 3 µg/ml human β<sub>2</sub>-  
microglobulin and 1 µg/ml P2S-12 peptide or control E75 peptide. In addition, T cells  
were simultaneously assayed on autologous fibroblasts transduced with the P502S gene  
30 or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the

fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

### EXAMPLE 9

#### ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES

##### IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts

retrovirally transduced to express P501S and CD8<sup>+</sup> lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (<sup>51</sup>Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

10

## EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN THE  
PROSTATE-SPECIFIC ANTIGEN P703P

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8<sup>+</sup> T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the

control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte  
5 cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures,  
10 CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

Studies identifying a further peptide epitope (referred to as peptide 4) derived from the prostate tumor-specific antigen P703P that is capable of being  
15 recognized by CD4 T cells on the surface of cells in the context of HLA class II molecules were carried out as follows. The amino acid sequence for peptide 4 is provided in SEQ ID NO: 781, with the corresponding cDNA sequence being provided in SEQ ID NO: 782.

Twenty 15-mer peptides overlapping by 10 amino acids and derived  
20 from the carboxy-terminal fragment of P703P were generated using standard procedures. Dendritic cells (DC) were derived from PBMC of a normal female donor using GM-CSF and IL-4 by standard protocols. CD4 T cells were generated from the same donor as the DC using MACS beads and negative selection. DC were pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration  
25 of 0.25 microgram/ml. Pulsed DC were washed and plated at  $1 \times 10^4$  cells/well of 96-well V-bottom plates and purified CD4 T cells were added at  $1 \times 10^5$ /well. Cultures were supplemented with 60 ng/ml IL-6 and 10 ng/ml IL-12 and incubated at 37 °C. Cultures were restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 u/ml IL-2.  
30 Following 4 *in vitro* stimulation cycles, 96 lines (each line corresponding to one well) were tested for specific proliferation and cytokine production in response to the

stimulating pools with an irrelevant pool of peptides derived from mammaglobin being used as a control.

One line (referred to as 1-F9) was identified from pool #1 that demonstrated specific proliferation (measured by <sup>3</sup>H proliferation assays) and cytokine production (measured by interferon-gamma ELISA assays) in response to pool #1 of P703P peptides. This line was further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and in HLA mismatch analyses to identify the relevant restricting allele. Line 1-F9 was found to specifically proliferate and produce interferon-gamma in response to peptide pool #1, and also to peptide 4 (SEQ ID NO: 781). Peptide 4 corresponds to amino acids 126-140 of SEQ ID NO: 327. Peptide titration experiments were conducted to assess the sensitivity of line 1-F9 for the specific peptide. The line was found to specifically respond to peptide 4 at concentrations as low as 0.25 ng/ml, indicating that the T cells are very sensitive and therefore likely to have high affinity for the epitope.

To determine the HLA restriction of the P703P response, a panel of antigen presenting cells (APC) was generated that was partially matched with the donor used to generate the T cells. The APC were pulsed with the peptide and used in proliferation and cytokine assays together with line 1-F9. APC matched with the donor at HLA-DRB0701 and HLA-DQB02 alleles were able to present the peptide to the T cells, indicating that the P703P-specific response is restricted to one of these alleles.

Antibody blocking assays were utilized to determine if the restricting allele was HLA-DR0701 or HLA-DQ02. The anti-HLA-DR blocking antibody L243 or an irrelevant isotype matched IgG2a were added to T cells and APC cultures pulsed with the peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) at 250 ng/ml. Standard interferon-gamma and proliferation assays were performed. Whereas the control antibody had no effect on the ability of the T cells to recognize peptide-pulsed APC, in both assays the anti-HLA-DR antibody completely blocked the ability of the T cells to specifically recognize peptide-pulsed APC.

To determine if the peptide epitope RMPTVLQCVNVS VVS (SEQ ID NO: 781) was naturally processed, the ability of line 1-F9 to recognize APC pulsed with recombinant P703P protein was examined. For these experiments a number of

recombinant P703P sources were utilized; *E. coli*-derived P703P, Pichia-derived P703P and baculovirus-derived P703P. Irrelevant protein controls used were *E. coli*-derived L3E (a lung-specific antigen) and baculovirus-derived mammaglobin. In interferon-gamma ELISA assays, line 1-F9 was able to efficiently recognize both *E. coli* forms of P703P as well as Pichia-derived recombinant P703P, while baculovirus-derived P703P was recognized less efficiently. Subsequent Western blot analysis revealed that the *E. coli* and Pichia P703P protein preparations were intact while the baculovirus P703P preparation was approximately 75% degraded. Thus, peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) from P703P is a naturally processed peptide epitope derived from P703P and presented to T cells in the context of HLA-DRB-0701

In further studies, twenty-four 15-mer peptides overlapping by 10 amino acids and derived from the N-terminal fragment of P703P (corresponding to amino acids 27-154 of SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was determined essentially as described above. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 10 microgram/ml. A large number of individual CD4 T cell lines (65/480) demonstrated significant proliferation and cytokine release (IFN-gamma) in response to the P703P peptide pools but not to a control peptide pool. The CD4 T cell lines which demonstrated specific activity were restimulated on the appropriate pool of P703P peptides and reassayed on the individual peptides of each pool as well as a peptide dose titration of the pool of peptides in a IFN-gamma release assay and in a proliferation assay.

Sixteen immunogenic peptides were recognized by the T cells from the entire set of peptide antigens tested. The amino acid sequences of these peptides are provided in SEQ ID NO: 799-814, with the corresponding cDNA sequences being provided in SEQ ID NO: 783-798, respectively. In some cases the peptide reactivity of the T cell line could be mapped to a single peptide, however some could be mapped to more than one peptide in each pool. Those CD4 T cell lines that displayed a representative pattern of recognition from each peptide pool with a reasonable affinity for peptide were chosen for further analysis (I-1A, -6A; II-4C, -5E; III-6E, IV-4B, -3F, -9B, -10F, V-5B, -4D, and -10F). These CD4 T cell lines were restimulated on the

appropriate individual peptide and reassayed on autologous DC pulsed with a truncated form of recombinant P703P protein made in *E. coli* (a.a. 96 - 254 of SEQ ID NO: 525), full-length P703P made in the baculovirus expression system, and a fusion between influenza virus NS1 and P703P made in *E. coli*. Of the T cell lines tested, line I-1A  
5 recognized specifically the truncated form of P703P (*E. coli*) but no other recombinant form of P703P. This line also recognized the peptide used to elicit the T cells. Line 2-4C recognized the truncated form of P703P (*E. coli*) and the full length form of P703P made in baculovirus, as well as peptide. The remaining T cell lines tested were either peptide-specific only (II-5E, II-6F, IV-4B, IV-3F, IV-9B, IV-10F, V-5B and V-4D) or  
10 were non-responsive to any antigen tested (V-10F). These results demonstrate that the peptide sequence RPLLANDLMLIKLDE (SEQ ID NO: 814; corresponding to a.a. 110-124 of SEQ ID NO: 525) recognized by the T cell line I-1A, and the peptide sequences SVSESDTIRSISIAS (SEQ ID NO: 811; corresponding to a.a. 125-139 of SEQ ID NO: 525) and ISIASQCPTAGNSCL (SEQ ID NO: 810; corresponding to a.a. 135-149 of  
15 SEQ ID NO: 525) recognized by the T cell line II-4C may be naturally processed epitopes of the P703P protein.

In further studies, forty 15-mer peptides overlapping by 10 amino acids and derived spanning amino acids 47 to 254 of P703P (SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was  
20 determined essentially as described above. DC were prepared from PBMC of a donor having distinct HLA DR and DQ alleles from that used in previous experiments. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 0.25 microgram/ml, and each pool containing 10 peptides. Twelve lines were identified that demonstrated specific proliferation and cytokine production  
25 (measured in gamma-interferon ELISA assays) in response to the stimulating peptide pool. These lines were further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and specific recognition of recombinant P703P protein. Lines 3A5H and 3A9H specifically proliferated and produced gamma-interferon in response to recombinant protein and one individual  
30 peptide as well as the peptide pool. Following re-stimulation on targets loaded with the specific peptide, only 3A9H responded specifically to targets exposed to lysates of

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fibroblasts infected adenovirus expressing full-length P703P. These results indicates that the line 3A9H can respond to antigenic peptide derived from protein synthesized in mammalian cells. The peptide to which the specific CD4 line responded correspond to amino acids 155-170 of P703P (SEQ ID NO: 943). The DNA sequence for this peptide  
5 is provided in SEQ ID NO: 942.

## EXAMPLE 11

EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN  
IN PROSTATE

10

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino  
15 acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is  
20 provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that  
25 B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach). Using real-time PCR on a panel of prostate tumors, expression of B305D in prostate tumors was shown to increase with increasing



Gleason grade, demonstrating that expression of B305D increases as prostate cancer progresses.

## EXAMPLE 12

### 5 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH THE PROSTATE-SPECIFIC ANTIGEN P501S

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996),  
10 human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- $\gamma$  ELISPOT analysis as described above. Using a panel of HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte  
15 cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3  $\mu$ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+  
20 T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon- $\gamma$  when stimulated with P501S and CD80-transduced autologous  
25 fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8<sup>+</sup> T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also

transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

A naturally processed, CD8, class I-restricted peptide epitope of P501S was identified as follows. Dendritic Cells (DC) were isolated by Percol gradient followed by differential adherence, and cultured for 5 days in the presence of RPMI medium containing 1% human serum, 50ng/ml GM-CSF and 30ng/ml IL-4. Following culture, DC were infected for 24 hours with P501S-expressing adenovirus at an MOI of 10 and matured for an additional 24 hours by the addition of 2ug/ml CD40 ligand. CD8 cells were enriched for by the subtraction of CD4+, CD14+ and CD16+ populations from PBMC with magnetic beads. Priming cultures containing 10,000 P501S-expressing DC and 100,000 CD8+ T cells per well were set up in 96-well V-bottom plates with RPMI containing 10% human serum, 5ng/ml IL-12 and 10ng/ml IL-6. Cultures were stimulated every 7 days using autologous fibroblasts retrovirally transduced to express P501S and CD80, and were treated with IFN-gamma for 48-72 hours to upregulate MHC Class I expression. 10u/ml IL-2 was added at the time of stimulation and on days 2 and 5 following stimulation. Following 4 stimulation cycles, one P501S-specific CD8+ T cell line (referred to as 2A2) was identified that produced IFN-gamma in response to IFN-gamma-treated P501S/CD80 expressing autologous fibroblasts, but not in response to IFN-gamma-treated P703P/CD80 expressing autologous fibroblasts in a  $\gamma$ -IFN Elispot assay. Line 2A2 was cloned in 96-well plates with 0.5 cell/well or 2 cells/well in the presence of 75,000 PBMC/well, 10,000 B-LCL/well, 30ng/ml OKT3 and 50u/ml IL-2. Twelve clones were isolated that showed strong P501S specificity in response to transduced fibroblasts.

Fluorescence activated cell sorting (FACS) analysis was performed on P501S-specific clones using CD3-, CD4- and CD8-specific antibodies conjugated to PercP, FITC and PE respectively. Consistent with the use of CD8 enriched T cells in the priming cultures, P5401S-specific clones were determined to be CD3+, CD8+ and  
5 CD4-.

To identify the relevant P501S epitope recognized by P501S specific CTL, pools of 18-20 mer or 30-mer peptides that spanned the majority of the amino acid sequence of P501S were loaded onto autologous B-LCL and tested in  $\gamma$ -IFN Elispot assays for the ability to stimulate two P501S-specific CTL clones, referred to as 4E5  
10 and 4E7. One pool, composed of five 18-20 mer peptides that spanned amino acids 411-486 of P501S (SEQ ID NO: 113), was found to be recognized by both P501S-specific clones. To identify the specific 18-20 mer peptide recognized by the clones, each of the 18-20 mer peptides that comprised the positive pool were tested individually in  $\gamma$ -IFN Elispot assays for the ability to stimulate the two P501S-specific CTL clones, 4E5 and  
15 4E7. Both 4E5 and 4E7 specifically recognized one 20-mer peptide (SEQ ID NO: 853; cDNA sequence provided in SEQ ID NO: 854) that spanned amino acids 453-472 of P501S. Since the minimal epitope recognized by CD8+ T cells is almost always either a 9 or 10-mer peptide sequence, 10-mer peptides that spanned the entire sequence of SEQ ID NO: 853 were synthesized that differed by 1 amino acid. Each of these 10-mer  
20 peptides was tested for the ability to stimulate two P501S-specific clones, (referred to as 1D5 and 1E12). One 10-mer peptide (SEQ ID NO: 855; cDNA sequence provided in SEQ ID NO: 856) was identified that specifically stimulated the P501S-specific clones. This epitope spans amino acids 463-472 of P501S. This sequence defines a minimal 10-mer epitope from P501S that can be naturally processed and to which CTL responses  
25 can be identified in normal PBMC. Thus, this epitope is a candidate for use as a vaccine moiety, and as a therapeutic and/or diagnostic reagent for prostate cancer.

To identify the class I restriction element for the P501S-derived sequence of SEQ ID NO: 855, HLA blocking and mismatch analyses were performed. In  $\gamma$ -IFN Elispot assays, the specific response of clones 4A7 and 4E5 to P501S-transduced  
30 autologous fibroblasts was blocked by pre-incubation with 25ug/ml W6/32 (pan-Class I blocking antibody) and B1.23.2 (HLA-B/C blocking antibody). These results

demonstrate that the SEQ ID NO: 855-specific response is restricted to an HLA-B or HLA-C allele.

For the HLA mismatch analysis, autologous B-LCL (HLA-A1,A2,B8,B51, Cw1, Cw7) and heterologous B-LCL (HLA-A2,A3,B18,B51,Cw5,Cw14) that share the HLAB51 allele were pulsed for one hour with 20ug/ml of peptide of SEQ ID NO: 855, washed, and tested in  $\gamma$ -IFN Elispot assays for the ability to stimulate clones 4A7 and 4E5. Antibody blocking assays with the B1.23.2 (HLA-B/C blocking antibody) were also performed. SEQ ID NO: 855-specific response was detected using both the autologous (D326) and heterologous (D107) B-LCL, and furthermore the responses were blocked by pre-incubation with 25ug/ml of B1.23.2 HLA-B/C blocking antibody. Together these results demonstrate that the P501S-specific response to the peptide of SEQ ID NO: 855 is restricted to the HLA-B51 class I allele. Molecular cloning and sequence analysis of the HLA-B51 allele from D3326 revealed that the HLA-B51 subtype of D326 is HLA-B51011.

Based on the 10-mer P501S-derived epitope of SEQ ID NO: 855, two 9-mers with the sequences of SEQ ID NO: 857 and 858 were synthesized and tested in Elispot assays for the ability to stimulate two P501S-specific CTL clones derived from line 2A2. The 10-mer peptide of SEQ ID NO: 855, as well as the 9-mer peptide of SEQ ID NO: 858, but not the 9-mer peptide of SEQ ID NO: 857, were capable of stimulating the P501S-specific CTL to produce IFN-gamma. These results demonstrate that the peptide of SEQ ID NO: 858 is a 9-mer P501S-derived epitope recognized by P501S-specific CTL. The DNA sequence encoding the epitope of SEQ ID NO: 858 is provided in SEQ ID NO: 859.

To identify the class I restricting allele for the P501S-derived peptide of SEQ ID NO: 855 and 858 specific response, each of the HLA B and C alleles were cloned from the donor used in the *in vitro* priming experiment. Sequence analysis indicated that the relevant alleles were HLA-B8, HLA-B51, HLA-Cw01 and HLA-Cw07. Each of these alleles were subcloned into an expression vector and co-transfected together with the P501S gene into VA-13 cells. Transfected VA-13 cells were then tested for the ability to specifically stimulate the P501S-specific CTL in ELISPOT assays. VA-13 cells transfected with P501S and HLA-B51 were capable of

stimulating the P501S-specific CTL to secrete gamma-IFN. VA-13 cells transfected with HLA-B51 alone or P501S + the other HLA-alleles were not capable of stimulating the P501S-specific CTL. These results demonstrate that the restricting allele for the P501S-specific response is the HLAB51 allele. Sequence analysis revealed that the  
5 subtype of the relevant restricting allele is HLA-B51011.

To determine if the P501S-specific CTL could recognize prostate tumor cells that express P501S, the P501S-positive lines LnCAP and CRL2422 (both expressing "moderate" amounts of P501S mRNA and protein), and PC-3 (expressing low amounts of P501S mRNA and protein), plus the P501S-negative cell line DU-145  
10 were retrovirally transduced with the HLA-B51011 allele that was cloned from the donor used to generate the P501S-specific CTL. HLA-B51011- or EGFP-transduced and selected tumor cells were treated with gamma-interferon and androgen (to upregulate stimulatory functions and P501S, respectively) and used in gamma-interferon Elispot assays with the P501S-specific CTL clones 4E5 and 4E7. Untreated  
15 cells were used as a control.

Both 4E5 and 4E7 efficiently and specifically recognized LnCAP and CRL2422 cells that were transduced with the HLA-B51011 allele, but not the same cell lines transduced with EGFP. Additionally, both CTL clones specifically recognized PC-3 cells transduced with HLA-B51011, but not the P501S-negative tumor cell line  
20 DU-145. Treatment with gamma-interferon or androgen did not enhance the ability of CTL to recognize tumor cells. These results demonstrate that P501S-specific CTL, generated by *in vitro* whole gene priming, specifically and efficiently recognize prostate tumor cell lines that express P501S.

A naturally processed CD4 epitope of P501S was identified as follows.

25 CD4 cells specific for P501S were prepared as described above. A series of 16 overlapping peptides were synthesized that spanned approximately 50% of the amino terminal portion of the P501S gene (amino acids 1- 325 of SEQ ID NO: 113). For priming, peptides were combined into pools of 4 peptides, pulsed at 4 µg/ml onto dendritic cells (DC) for 24 hours, with TNF-alpha. DC were then washed and mixed  
30 with negatively selected CD4+ T cells in 96 well U-bottom plates. Cultures were re-stimulated weekly on fresh DC loaded with peptide pools. Following a total of 4

stimulation cycles, cells were rested for an additional week and tested for specificity to APC pulsed with peptide pools using  $\gamma$ -IFN ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool at 4 $\mu$ g/ml or an irrelevant peptide at  $\mu$ g/ml were used as APC. T cell lines that demonstrated either  
5 specific cytokine secretion or proliferation were then tested for recognition of individual peptides that were present in the pool. T cell lines could be identified from pools A and B that recognized individual peptides from these pools.

From pool A, lines AD9 and AE10 specifically recognized peptide 1 (SEQ ID NO: 862), and line AF5 recognized peptide 39 (SEQ ID NO: 861). From pool  
10 B, line BC6 could be identified that recognized peptide 58 (SEQ ID NO: 860). Each of these lines were stimulated on the specific peptide and tested for specific recognition of the peptide in a titration assay as well as cell lysates generated by infection of HEK 293 cells with adenovirus expressing either P501S or an irrelevant antigen. For these assays, APC-adherent monocytes were pulsed with either 10, 1, or 0.1  $\mu$ g/ml individual P501S  
15 peptides, and DC were pulsed overnight with a 1:5 dilution of adenovirally infected cell lysates. Lines AD9, AE10 and AF5 retained significant recognition of the relevant P501S-derived peptides even at 0.1 mg/ml. Furthermore, line AD9 demonstrated significant (8.1 fold stimulation index) specific activity for lysates from adenovirus-P501S infected cells. These results demonstrate that high affinity CD4 T cell lines can  
20 be generated toward P501S-derived epitopes, and that at least a subset of these T cells specific for the P501S derived sequence of SEQ ID NO: 862 are specific for an epitope that is naturally processed by human cells. The DNA sequences encoding the amino acid sequences of SEQ ID NO: 860-862 are provided in SEQ ID NO: 863-865, respectively.

25 To further characterize the P501S-specific activity of AD9, the line was cloned using anti-CD3. Three clones, referred to as 1A1, 1A9 and 1F5, were identified that were specific for the P501S-1 peptide (SEQ ID NO: 862). To determine the HLA restriction allele for the P501S-specific response, each of these clones was tested in class II antibody blocking and HLA mismatch assays using proliferation and gamma-  
30 interferon assays. In antibody blocking assays and measuring gamma-interferon production using ELISA assays, the ability of all three clones to recognize peptide

pulsed APC was specifically blocked by co-incubation with either a pan-class II blocking antibody or a HLA-DR blocking antibody, but not with a HLA-DQ or an irrelevant antibody. Proliferation assays performed simultaneously with the same cells confirmed these results. These data indicate that the P501S-specific response of the clones is restricted by an HLA-DR allele. Further studies demonstrated that the restricting allele for the P501S-specific response is HLA-DRB1501.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

##### BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.



**Table I**  
**Summary of Prostate Tumor Antigens**

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-idoitol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein. (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other

normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 (also referred to as P553S) showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

Subsequent full-length cloning studies on P553S, using standard techniques, revealed that this clone is an incomplete spliced form of P501S. The determined cDNA sequences for four splice variants of P553S are provided in SEQ ID NO: 702-705. An amino acid sequence encoded by SEQ ID NO: 705 is provided in SEQ ID NO: 706. The cDNA sequence of SEQ ID NO: 702 was found to contain two open reading frames (ORFs). The amino acid sequences encoded by these two ORFs are provided in SEQ ID NO: 707 and 708.

#### EXAMPLE 14

##### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table IIProstate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

- 5 Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the
- 10 Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters
- 15 (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table IIIProstate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

5           The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels

10 of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes

15 generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The

20 sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV

Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

Further studies on the clone of SEQ ID NO: 407 (also referred to as P1020C) led to the isolation of an extended cDNA sequence provided in SEQ ID NO: 591. This extended cDNA sequence was found to contain an open reading frame that  
5 encodes the predicted amino acid sequence of SEQ ID NO: 592. The P1020C cDNA and amino acid sequences were found to show some similarity to the human endogenous retroviral HERV-K pol gene and protein.

#### EXAMPLE 15

##### 10 FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above  
15 was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-460 represent novel genes. The others (SEQ ID NO: 454-  
20 458 and 461-467) correspond to known sequences. Comparison of the determined



cDNA sequence of SEQ ID NO: 461 with sequences in the Genbank database using the BLAST program revealed homology to the previously identified transmembrane protease serine 2 (TMPRSS2). The full-length cDNA sequence for this clone is provided in SEQ ID NO: 894, with the corresponding amino acid sequence being  
5 provided in SEQ ID NO: 895. The cDNA sequence encoding the first 209 amino acids of TMPRSS2 is provided in SEQ ID NO: 896, with the first 209 amino acids being provided in SEQ ID NO: 897.

The sequence of SEQ ID NO: 462 (referred to as P835P) was found to correspond to the previously identified clone FLJ13518 (Accession AK023643; SEQ ID  
10 NO: 917), which had no associated open reading frame (ORF). This clone was used to search the Geneseq DNA database and matched a clone previously identified as a G protein-coupled receptor protein (DNA Geneseq Accession A09351; amino acid Geneseq Accession Y92365), that is characterized by the presence of seven transmembrane domains. The sequences of fragments between these domains are  
15 provided in SEQ ID NO: 921-928, with SEQ ID NO: 921, 923, 925 and 927 representing extracellular domains and SEQ ID NO: 922, 924, 926 and 928 representing intracellular domains. SEQ ID NO: 921-928 represent amino acids 1-28, 53-61, 83-103, 124-143, 165-201, 226-238, 263-272 and 297-381, respectively, of P835P. The full-length cDNA sequence for P835P is provided in SEQ ID NO: 916. The cDNA  
20 sequence of the open reading frame for P835P, including stop codon, is provided in SEQ ID NO: 918, with the open reading frame without stop codon being provided in SEQ ID NO: 919 and the corresponding amino acid sequence being provided in SEQ ID NO: 920.

25

## EXAMPLE 16

## FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P  
30 fragment described above. One million colonies were plated on LB/Ampicillin plates.

Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene. Subsequent comparison of the cDNA sequences of P710P with those in Genbank revealed homology to the DD3 gene (Genbank accession numbers AF103907 & AF103908). The cDNA sequence of DD3 is provided in SEQ ID NO: 690.

#### EXAMPLE 17

##### PROTEIN EXPRESSION OF PROSTATE-SPECIFIC ANTIGENS

This example describes the expression and purification of prostate-specific antigens in *E. coli*, baculovirus and mammalian cells.

##### a) Expression of P501S in *E. coli*

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was

cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The  
5 resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression  
10 was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen  
15 Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as  
20 Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to  
25 aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of  
30 the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S

DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The  
5 sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C  
10 fusion was used for expression in BL21CodonPlus induced by CE6 phage.

A fusion construct comprising a fragment of P501S (amino acids 36-298 of SEQ ID NO: 113) located down-stream of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 848) was prepared as follows. P501S DNA was used to perform PCR using the primers AW042 (SEQ ID NO: 849) and AW053 (SEQ ID NO: 850). AW042 is a sense  
15 cloning primer that contains a EcoRI site. AW053 is an antisense primer with stop and Xho I sites. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the EcoRI and Xho I sites. The resulting fusion construct (referred to as Ra12-P501S-E2) was expressed in B834 (DE3) pLys S *E. coli* host cells in TB media for 2 h at room temperature. Expressed protein  
20 was purified by washing the inclusion bodies and running on a Ni-NTA column. The purified protein stayed soluble in buffer containing 20 mM Tris-HCl (pH 8), 100 mM NaCl, 10 mM  $\beta$ -Me and 5% glycerol. The determined cDNA and amino acid sequences for the expressed fusion protein are provided in SEQ ID NO: 851 and 852, respectfully.

25 b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the

manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

#### c) Expression of P501S in mammalian cells

Full-length P501S (553 amino acids; SEQ ID NO: 113) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The

Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15  $\mu$ l of GenePorter was diluted in 500  $\mu$ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2  $\mu$ g of plasmid DNA that was diluted in 500  $\mu$ l of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

#### d) Expression of P703P in Baculovirus

The cDNA for full-length P703P-DE5 (SEQ ID NO: 326), together with several flanking restriction sites, was obtained by digesting the plasmid pCDNA703 with restriction endonucleases Xba I and Hind III. The resulting restriction fragment (approx. 800 base pairs) was ligated into the transfer plasmid pFastBacI which was digested with the same restriction enzymes. The sequence of the insert was confirmed by DNA sequencing. The recombinant transfer plasmid pFBP703 was used to make recombinant bacmid DNA and baculovirus using the Bac-To-Bac Baculovirus expression system (BRL Life Technologies). High Five cells were infected with the recombinant virus BVP703, as described above, to obtain recombinant P703P protein.

e) Expression of P788P in *E. Coli*

A truncated, N-terminal portion, of P788P (residues 1-644 of SEQ ID NO: 777; referred to as P788P-N) fused with a C-terminal 6xHis Tag was expressed in *E. coli* as follows. P788P cDNA was amplified using the primers AW080 and AW081 (SEQ ID NO: 815 and 816). AW080 is a sense cloning primer with an NdeI site. AW081 is an antisense cloning primer with a XhoI site. The PCR-amplified P788P, as well as the vector pCRX1, were digested with NdeI and XhoI. Vector and insert were ligated and transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. P788P-N clone #6 was confirmed to be identical to the designed construct. The expression construct P788P-N #6/pCRX1 was transformed into *E. coli* BL21 CodonPlus-RIL competent cells. After induction, most of the cells grew well, achieving OD600 of greater than 2.0 after 3 hr. Coomassie stained SDS-PAGE showed an over-expressed band at about 75 kD. Western blot analysis using a 6xHisTag antibody confirmed the band was P788P-N. The determined cDNA sequence for P788P-N is provided in SEQ ID NO: 817, with the corresponding amino acid sequence being provided in SEQ ID NO: 818.

f) Expression of P510S in *E. coli*

The P510S protein has 9 potential transmembrane domains and is predicted to be located at the plasma membrane. The C-terminal protein of this protein, as well as the predicted third extracellular domain of P510S were expressed in *E. coli* as follows.

The expression construct referred to as Ra12-P501S-C was designed to have a 6 HisTag at the N-terminal end, followed by the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and then the C-terminal portion of P510S (amino residues 1176-1261 of SEQ ID NO: 538). Full-length P510S was used to amplify the P510S-C fragment by PCR using the primers AW056 and AW057 (SEQ ID NO: 820 and 821, respectively). AW056 is a sense cloning primer with an EcoRI site. AW057 is an antisense primer with stop and XhoI sites. The amplified P501S fragment and Ra12/pCRX1 were digested with EcoRI and XhoI and then purified. The insert and

vector were ligated together and transformed into NovaBlue. Colonies were randomly screened for insert and sequences. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. A mini-induction screen was performed to optimize the expression conditions. After induction

5 the cells grew well, achieving OD 600 nm greater than 2.0 after 3 hours. Coomassie stain SDS-PAGE showed a highly over-expressed band at approx. 30 kD. Though this is higher than the expected molecular weight, western blot analysis was positive, showing this band to be the His tag-containing protein. The optimized culture conditions are as follows. Dilute overnight culture/daytime culture (LB + kanamycin +

10 chloramphenicol) into 2xYT (with kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2xYT. Allow to grow at 37 °C until OD600 = 0.6. Take an aliquot out as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down cells and store at -80 °C. The determined cDNA and amino acid sequences for the Ra12-P510S-C construct are provided in SEQ ID NO: 822 and 825,

15 respectively.

The expression construct P510S-C was designed to have a 5' added start codon and a glycine (GGA) codon and then the P510S C terminal fragment followed by the in frame 6x histidine tag and stop codon from the pET28b vector. The cloning strategy is similar to that used for Ra12-P510S-C, except that the PCR primers

20 employed were those shown in SEQ ID NO: 828 and 829, respectively and the NcoI/XhoI cut in pET28b was used. The primer of SEQ ID NO: 828 created a 5' NcoI site and added a start codon. The antisense primer of SEQ ID NO: 829 creates a XhoI site on P510S C terminal fragment. Clones were confirmed by sequencing. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3)

25 CodonPlus-RIL competent cells. An OD600 of greater than 2.0 was obtained 30 hours after induction. Coomassie stained SDS-PAGE showed an over-expressed band at about 11 kD. Western blot analysis confirmed that the band was P510S-C, as did N-terminal protein sequencing. The optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (+

30 kanamycin and chloramphenicol) at a ratio of 25 mL culture to 1 liter 2x YT, and allow



to grow at 37 °C until an OD 600 of about 0.5 is reached. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-C construct are shown in SEQ ID NO: 823 and 826, respectively.

5           The predicted third extracellular domain of P510S (P510S-E3; residues 328-676 of SEQ ID NO: 538) was expressed in *E. coli* as follows. The P510S fragment was amplified by PCR using the primers shown in SEQ ID NO: 830 and 831. The primer of SEQ ID NO: 830 is a sense primer with an NdeI site for use in ligating into pPDM. The primer of SEQ ID NO: 831 is an antisense primer with an added XhoI site  
10 for use in ligating into pPDM. The resulting fragment was cloned to pPDM at the NdeI and XhoI sites. Clones were confirmed by sequencing. For protein expression, the clone was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. After induction, an OD600 of greater than 2.0 was achieved after 3 hours. Coomassie stained SDS-PAGE showed an over-expressed band at about 39 kD, and N-terminal sequencing  
15 confirmed the N-terminal to be that of P510S-E3. Optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2x YT. Allow to grow at 37 °C until OD 600 equals 0.6. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3  
20 sample, spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P501S-E3 construct are provided in SEQ ID NO: 824 and 827, respectively.

g) Expression of P775S in *E. Coli*

25           The antigen P775P contains multiple open reading frames (ORF). The third ORF, encoding the protein of SEQ ID NO: 483, has the best motif score. An expression fusion construct containing the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and P775P-ORF3 with an N-terminal 6x HisTag was prepared as follows. P775P-ORF3 was amplified using the sense PCR primers of SEQ ID NO: 832 and the anti-sense PCR primer of SEQ ID NO: 833. The PCR amplified fragment of P775P and

Ra12/pCRX1 were digested with the restriction enzymes EcoRI and XhoI. Vector and insert were ligated and then transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. A clone having the desired sequence was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. Two hours after induction, the cell density peaked at OD600 of approximately 1.8. Coomassie stained SDS-PAGE showed an over-expressed band at about 31 kD. Western blot using 6x HisTag antibody confirmed that the band was Ra12-P775P-ORF3. The determined cDNA and amino acid sequences for the fusion construct are provided in SEQ ID NO: 834 and 835, respectively.

H) Expression of a P703P His tag fusion protein in *E. coli*

The cDNA for the coding region of P703P was prepared by PCR using the primers of SEQ ID NO: 836 and 837. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P703P are provided in SEQ ID NO: 838 and 839, respectively.

I) Expression of a P705P His tag fusion protein in *E. coli*

The cDNA for the coding region of P705P was prepared by PCR using the primers of SEQ ID NO: 840 and 841. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P705P are provided in SEQ ID NO: 842 and 843, respectively.

J) Expression of a P711P His tag fusion protein in *E. coli*

The cDNA for the coding region of P711P was prepared by PCR using the primers of SEQ ID NO: 844 and 845. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P711P are provided in SEQ ID NO: 846 and 847, respectively.

K) Expression of P767P in *E. coli*

The full-length coding region of P767P (amino acids 2-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-468 and PDM-469 (SEQ ID NO: 935 and 936, respectively). DNA amplification was performed using 10 µl 10X Pfu buffer, 1 µl 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 66°C for 15 sec and by 72°C for 2 min., and lastly by 1 cycle of 72°C for 4 min. The PCR product was digested with XhoI and cloned into a modified pET28 vector with a histidine tag in frame on the 5' end that was digested with Eco72I and XhoI. The construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The cDNA coding region for the recombinant B767P protein is provided in SEQ ID NO: 938, with the corresponding amino acid sequence being provided in SEQ ID NO: 941. The full-length P767P did not express at high enough levels for detection or purification.

A truncated coding region of P767P (referred to as B767P-B; amino acids 47-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-573 and PDM-469 (SEQ ID NO: 937 and 936, respectively) and the PCR conditions described above for full-length P767P. The PCR product was digested with XhoI and cloned into the modified pET28 vector that was digested with Eco72I and XhoI. The

construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The protein was found to be expressed in the inclusion body pellet. The coding region for the expressed B767P-B protein is provided in SEQ ID NO: 939, with the corresponding amino acid sequence  
5 being provided in SEQ ID NO: 940.

### EXAMPLE 18

#### PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

10

##### a) Preparation and Characterization of Polyclonal Antibodies against P703P, P504S and P509S

Polyclonal antibodies against P703P, P504S and P509S were prepared as follows.

15 Each prostate tumor antigen expressed in an *E. coli* recombinant expression system was grown overnight in LB broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml to 2x YT plus appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the Optical Density (at 560 nm) of the culture reached 0.4-0.6, the cells were  
20 induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation. The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty ml of lysis buffer was added to the cell pellets and vortexed. To break open the *E. coli* cells, this mixture was then run  
25 through the French Press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein. For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed

inclusion body pellet was solubilized with either 8 M urea or 6 M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 min to 1 hour at room temperature with continuous agitation. After incubation, the resin and protein mixture were poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

As a final purification step, a strong anion exchange resin such as HiPrepQ (Biorad) was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with a increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool. The pooled fractions were dialyzed against 10 mM Tris pH 8.0. The proteins were then viald after filtration through a 0.22 micron filter and the antigens were frozen until needed for immunization.

Four hundred micrograms of each prostate antigen was combined with 100 micrograms of muramyl dipeptide (MDP). Every four weeks rabbits were boosted with 100 micrograms mixed with an equal volume of Incomplete Freund's Adjuvant (IFA). Seven days following each boost, the animal was bled. Sera was generated by incubating the blood at 4°C for 12-4 hours followed by centrifugation.

Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) of recombinant protein at 4 °C for 20 hours. 250 microliters of BSA blocking buffer was added to the wells and incubated at room temperature for 2 hours. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS. Fifty microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000 dilution was added and incubated at room temperature for 30 min. Plates were again

washed as described above and 100 microliters of TMB microwell peroxidase substrate was added to each well. Following a 15 min incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H<sub>2</sub>SO<sub>4</sub> and read immediately at 450 nm. All polyclonal antibodies showed immunoreactivity to the appropriate antigen.

b) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ( $\mu\text{g/ml}$ )
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

- 5                   The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1  $\mu\text{g/ml}$ , followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using
- 10 an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-
- 15 LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described

above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled anti-



mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors,

5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

c) Preparation and Characterization of Antibodies against P503S

5 A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at  
10 Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur

fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

#### d) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM

technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

5

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

10

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-  
15 514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk<sup>-/-</sup> cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated  
20 from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight  
25 since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure

specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using  
5 anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

e) Preparation and Characterization of Antibodies against P504S

Full-length P504S (SEQ ID NO: 108) was expressed and purified from  
10 bacteria essentially as described above for P501S and employed to raise rabbit monoclonal antibodies using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). The anti-P504S monoclonal antibody 13H4 was shown by Western blot to bind to both expressed recombinant P504S and to native P504S in tumor cells.

15 Immunohistochemical studies using 13H4 to assess P504S expression in various prostate tissues were performed as described above. A total of 104 cases, including 65 cases of radical prostatectomies with prostate cancer (PC), 26 cases of prostate biopsies and 13 cases of benign prostate hyperplasia (BPH), were stained with the anti-P504S monoclonal antibody 13H4. P504S showed strongly cytoplasmic  
20 granular staining in 64/65 (98.5%) of PCs in prostatectomies and 26/26 (100%) of PCs in prostatic biopsies. P504S was stained strongly and diffusely in carcinomas (4+ in 91.2% of cases of PC; 3+ in 5.5%; 2+ in 2.2% and 1+ in 1.1%) and high grade prostatic intraepithelial neoplasia (4+ in all cases). The expression of P504S did not vary with Gleason score. Only 17/91 (18.7%) of cases of NP/BPH around PC and 2/13 (15.4%) of  
25 BPH cases were focally (1+, no 2+ to 4+ in all cases) and weakly positive for P504S in large glands. Expression of P504S was not found in small atrophic glands, postatrophic hyperplasia, basal cell hyperplasia and transitional cell metaplasia in either biopsies or prostatectomies. P504S was thus found to be over-expressed in all Gleason scores of prostate cancer (98.5 to 100% of sensitivity) and exhibited only focal positivities in

large normal glands in 19/104 of cases (82.3% of specificity). These findings indicate that P504S may be usefully employed for the diagnosis of prostate cancer.

### EXAMPLE 19

#### CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A

Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether.

- 5 The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described
- 10 above.

- Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell
- 15 sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and
- 20 stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (*i.e.*, intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

- 25 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun
- 30 at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C.



Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of

SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

In further studies, mouse monoclonal antibodies were raised against amino acids 296 to 322 to P501S, which are predicted to be in an extracellular domain. A/J mice were immunized with P501S/adenovirus, followed by subsequent boosts with an *E. coli* recombinant protein, referred to as P501N, that contains amino acids 296 to 322 of P501S, and with peptide 296-322 (SEQ ID NO: 898) coupled with KLH. The mice were subsequently used for splenic B cell fusions to generate anti-peptide hybridomas. The resulting 3 clones, referred to as 4F4 (IgG1,kappa), 4G5 (IgG2a,kappa) and 9B9 (IgG1,kappa), were grown for antibody production. The 4G5 mAb was purified by passing the supernatant over a Protein A-sepharose column,

followed by antibody elution using 0.2M glycine, pH 2.3. Purified antibody was neutralized by the addition of 1M Tris, pH 8, and buffer exchanged into PBS.

For ELISA analysis, 96 well plates were coated with P501S peptide 296-322 (referred to as P501-long), an irrelevant P775 peptide, P501S-N, P501TR2, P501S-long-KLH, P501S peptide 306-319 (referred to as P501-short)-KLH, or the irrelevant peptide 2073-KLH, all at a concentration of 2 ug/ml and allowed to incubate for 60 minutes at 37 °C. After coating, plates were washed 5X with PBS + 0.1% Tween and then blocked with PBS, 0.5% BSA, 0.4% Tween20 for 2 hours at room temperature. Following the addition of supernatants or purified mAb, the plates were incubated for 60 minutes at room temperature. Plates were washed as above and donkey anti-mouse IgHRP-linked secondary antibody was added and incubated for 30 minutes at room temperature, followed by a final washing as above. TMB peroxidase substrate was added and incubated 15 minutes at room temperature in the dark. The reaction was stopped by the addition of 1N H<sub>2</sub>SO<sub>4</sub> and the OD was read at 450 nM. All three hybrid clones secreted mAb that recognized peptide 296-322 and the recombinant protein P501N.

For FACS analysis, HEK293 cells were transiently transfected with a P501S/VR1012 expression constructs using Fugene 6 reagent. After 2 days of culture, cells were harvested and washed, then incubated with purified 4G5 mAb for 30 minutes on ice. After several washes in PBS, 0.5% BSA, 0.01% azide, goat anti-mouse Ig-FITC was added to the cells and incubated for 30 minutes on ice. Cells were washed and resuspended in wash buffer including 1% propidium iodide and subjected to FACS analysis. The FACS analysis confirmed that amino acids 296-322 of P501S are in an extracellular domain and are cell surface expressed.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server

(<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al.* 5 *Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

## EXAMPLE 20

### REGULATION OF EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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Steroid (androgen) hormone modulation is a common treatment modality in prostate cancer. The expression of a number of prostate tissue-specific antigens have previously been demonstrated to respond to androgen. The responsiveness of the prostate-specific antigen P501S to androgen treatment was examined in a tissue culture 15 system as follows.

Cells from the prostate tumor cell line LNCaP were plated at  $1.5 \times 10^6$  cells/T75 flask (for RNA isolation) or  $3 \times 10^5$  cells/well of a 6-well plate (for FACS analysis) and grown overnight in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum (BRL Life Technologies, Gaithersburg, MD). Cell culture was 20 continued for an additional 72 hours in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum, with 1 nM of the synthetic androgen Methyltrienolone (R1881; New England Nuclear) added at various time points. Cells were then harvested for RNA isolation and FACS analysis at 0, 1, 2, 4, 8, 16, 24, 28 and 72-hours post androgen addition. FACS analysis was performed using the anti-P501S antibody 10E3- 25 G4-D3 and permeabilized cells.

For Northern analysis, 5-10 micrograms of total RNA was run on a formaldehyde denaturing gel, transferred to Hybond-N nylon membrane (Amersham Pharmacia Biotech, Piscataway, NJ), cross-linked and stained with methylene blue. The filter was then prehybridized with Church's Buffer (250 mM  $\text{Na}_2\text{HPO}_4$ , 70 mM  $\text{H}_3\text{PO}_4$ , 30 1 mM EDTA, 1% SDS, 1% BSA in pH 7.2) at 65 °C for 1 hour. P501S DNA was

labeled with  $^{32}\text{P}$  using High Prime random-primed DNA labeling kit (Boehringer Mannheim). Unincorporated label was removed using MicroSpin S300-HR columns (Amersham Pharmacia Biotech). The RNA filter was then hybridized with fresh Church's Buffer containing labeled cDNA overnight, washed with 1X SCP (0.1 M NaCl, 0.03 M  $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ , 0.001 M  $\text{Na}_2\text{EDTA}$ ), 1% sarkosyl (n-lauroylsarcosine) and exposed to X-ray film.

Using both FACS and Northern analysis, P501S message and protein levels were found to increase in response to androgen treatment.

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## EXAMPLE 21

## PREPARATION OF FUSION PROTEINS OF PROSTATE-SPECIFIC ANTIGENS

The example describes the preparation of a fusion protein of the prostate-specific antigen P703P and a truncated form of the known prostate antigen PSA. The truncated form of PSA has a 21 amino acid deletion around the active serine site. The expression construct for the fusion protein also has a restriction site at 3' end, immediately prior to the termination codon, to aid in adding cDNA for additional antigens.

The full-length cDNA for PSA was obtained by RT-PCR from a pool of RNA from human prostate tumor tissues using the primers of SEQ ID NO: 607 and 608, and cloned in the vector pCR-Blunt II-TOPO. The resulting cDNA was employed as a template to make two different fragments of PSA by PCR with two sets of primers (SEQ ID NO: 609 and 610; and SEQ ID NO: 611 and 612). The PCR products having the expected size were used as templates to make truncated forms of PSA by PCR with the primers of SEQ ID NO: 611 and 613, which generated PSA (delta 208-218 in amino acids). The cDNA for the mature form of P703P with a 6X histidine tag at the 5' end, was prepared by PCR with P703P and the primers of SEQ ID NO: 614 and 615. The cDNA for the fusion of P703P with the truncated form of PSA (referred to as FOPP) was then obtained by PCR using the modified P703P cDNA and the truncated form of PSA cDNA as templates and the primers of SEQ ID NO: 614 and 615. The FOPP

cDNA was cloned into the NdeI site and XhoI site of the expression vector pCRX1, and confirmed by DNA sequencing. The determined cDNA sequence for the fusion construct FOPP is provided in SEQ ID NO: 616, with the amino acid sequence being provided in SEQ ID NO: 617.

5               The fusion FOPP was expressed as a single recombinant protein in *E. coli* as follows. The expression plasmid pCRX1FOPP was transformed into the *E. coli* strain BL21-CodonPlus RIL. The transformant was shown to express FOPP protein upon induction with 1 mM IPTG. The culture of the corresponding expression clone was inoculated into 25 ml LB broth containing 50 ug/ml kanamycin and 34 ug/ml  
10 chloramphenicol, grown at 37 °C to OD600 of about 1, and stored at 4 °C overnight. The culture was diluted into 1 liter of TB LB containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, and grown at 37 °C to OD600 of 0.4. IPTG was added to a final concentration of 1 mM, and the culture was incubated at 30 °C for 3 hours. The cells were pelleted by centrifugation at 5,000 RPM for 8 min. To purify the protein, the  
15 cell pellet was suspended in 25 ml of 10 mM Tris-Cl pH 8.0, 2mM PMSF, complete protease inhibitor and 15 ug lysozyme. The cells were lysed at 4 °C for 30 minutes, sonicated several times and the lysate centrifuged for 30 minutes at 10,000 x g. The precipitate, which contained the inclusion body, was washed twice with 10 mM Tris-Cl pH 8.0 and 1% CHAPS. The inclusion body was dissolved in 40 ml of 10 mM Tris-Cl  
20 pH 8.0, 100 mM sodium phosphate and 8 M urea. The solution was bound to 8 ml Ni-NTA (Qiagen) for one hour at room temperature. The mixture was poured into a 25 ml column and washed with 50 ml of 10 mM Tris-Cl pH 6.3, 100 mM sodium phosphate, 0.5% DOC and 8M urea. The bound protein was eluted with 350 mM imidazole, 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The fractions containing  
25 FOPP proteins were combined and dialyzed extensively against 10 mM Tris-Cl pH 4.6, aliquoted and stored at -70 °C.

## EXAMPLE 22

REAL-TIME PCR CHARACTERIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S IN  
PERIPHERAL BLOOD OF PROSTATE CANCER PATIENTS

5           Circulating epithelial cells were isolated from fresh blood of normal individuals and metastatic prostate cancer patients, mRNA isolated and cDNA prepared using real-time PCR procedures. Real-time PCR was performed with the Taqman<sup>TM</sup> procedure using both gene specific primers and probes to determine the levels of gene expression.

10           Epithelial cells were enriched from blood samples using an immunomagnetic bead separation method (Dynal A.S., Oslo, Norway). Isolated cells were lysed and the magnetic beads removed. The lysate was then processed for poly A+ mRNA isolation using magnetic beads coated with Oligo(dT)25. After washing the beads in buffer, bead/poly A+ RNA samples were suspended in 10 mM Tris HCl pH 8.0  
15 and subjected to reversed transcription. The resulting cDNA was subjected to real-time PCR using gene specific primers. Beta-actin content was also determined and used for normalization. Samples with P501S copies greater than the mean of the normal samples + 3 standard deviations were considered positive. Real time PCR on blood samples was performed using the Taqman<sup>TM</sup> procedure but extending to 50 cycles using  
20 forward and reverse primers and probes specific for P501S. Of the eight samples tested, 6 were positive for P501S and  $\beta$ -actin signal. The remaining 2 samples had no detectable  $\beta$ -actin or P501S. No P501S signal was observed in the four normal blood samples tested.

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## EXAMPLE 23

EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGENS P703P AND P501S IN  
SCID MOUSE-PASSAGED PROSTATE TUMORS

30           When considering the effectiveness of antigens in the treatment of prostate cancer, the continued presence of the antigens in tumors during androgen

ablation therapy is important. The presence of the prostate-specific antigens P703P and P501S in prostate tumor samples grown in SCID mice in the presence of testosterone was evaluated as follows.

Two prostate tumors that had metastasized to the bone were removed from patients, implanted into SCID mice and grown in the presence of testosterone. Tumors were evaluated for mRNA expression of P703P, P501S and PSA using quantitative real time PCR with the SYBR green assay method. Expression of P703P and P501S in a prostate tumor was used as a positive control and the absence in normal intestine and normal heart as negative controls. In both cases, the specific mRNA was present in late passage tumors. Since the bone metastases were grown in the presence of testosterone, this implies that the presence of these genes would not be lost during androgen ablation therapy.

#### EXAMPLE 24

##### ANTI-P503S MONOCLONAL ANTIBODY INHIBITS TUMOR GROWTH *IN VIVO*

The ability of the anti-P503S monoclonal antibody 20D4 to suppress tumor formation in mice was examined as follows.

Ten SCID mice were injected subcutaneously with HEK293 cells that expressed P503S. Five mice received 150 micrograms of 20D4 intravenously at day 0 (time of tumor cell injection), day 5 and day 9. Tumor size was measured for 50 days. Of the five animals that received no 20D4, three formed detectable tumors after about 2 weeks which continued to enlarge throughout the study. In contrast, none of the five mice that received 20D4 formed tumors. These results demonstrate that the anti-P503S Mab 20D4 displays potent anti-tumor activity *in vivo*.

#### EXAMPLE 25

##### CHARACTERIZATION OF A T CELL RECEPTOR CLONE FROM A P501S-SPECIFIC T CELL CLONE

T cells have a limited lifespan. However, cloning of T cell receptor (TCR) chains and subsequent transfer essentially enables infinite propagation of the T



cell specificity. Cloning of tumor-antigen TCR chains allows the transfer of the specificity into T cells isolated from patients that share the TCR MHC-restricting allele. Such T cells could then be expanded and used in adoptive transfer settings to introduce the tumor antigen specificity into patients carrying tumors that express the antigen. T cell receptor alpha and beta chains from a CD8 T cell clone specific for the prostate-specific antigen P501S were isolated and sequenced as follows.

Total mRNA from  $2 \times 10^6$  cells from CTL clone 4E5 (described above in Example 12) was isolated using Trizol reagent and cDNA was synthesized. To determine Va and Vb sequences in this clone, a panel of Va and Vb subtype-specific primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of the clones expressed a common Vb sequence that corresponded to the Vb7 subfamily. Furthermore, using cDNA generated from the clone, the Va sequence expressed was determined to be Va6. To clone the full TCR alpha and beta chains from clone 4E5, primers were designed that spanned the initiator and terminator-coding TCR nucleotides. The primers were as follows: TCR Valpha-6 5'(sense): GGATCC---GCCGCCACC---ATGTCACCTTCTAGCCTGCT (SEQ ID NO: 899) BamHI site Kozak TCR alpha sequence TCR alpha 3' (antisense): GTCGAC---TCAGCTGGACCACAGCCGCAG (SEQ ID NO: 900) Sall site TCR alpha constant sequence TCR Vbeta-7. 5'(sense): GGATCC---GCCGCCACC---ATGGGCTGCAGGCTGCTCT (SEQ ID NO: 901) BamHI site Kozak TCR alpha sequence TCR beta 3' (antisense): GTCGAC---TCAGAAATCCTTTCTCTTGAC (SEQ ID NO: 902) Sall site TCR beta constant sequence. Standard 35 cycle RT-PCR reactions were established using cDNA synthesized from the CTL clone and the above primers, employing the proofreading thermostable polymerase PWO (Roche, Nutley, NJ).

The resultant specific bands (approx. 850 bp for alpha and approx. 950 for beta) were ligated into the PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids containing full-length alpha and beta chains were identified, and large scale preparations of the corresponding plasmids were generated. Plasmids containing full-length TCR alpha and beta chains were submitted

for sequencing. The sequencing reactions demonstrated the cloning of full-length TCR alpha and beta chains with the determined cDNA sequences for the Vb and Va chains being shown in SEQ ID NO: 903 and 904, respectively. The corresponding amino acid sequences are shown in SEQ ID NO: 905 and 906, respectively. The Va sequence was shown by nucleotide sequence alignment to be 99% identical (347/348) to Va6.2, and the Vb to be 99% identical to Vb7 (336/338).

### EXAMPLE 26

#### CAPTURE OF PROSTATE SPECIFIC CELLS USING

#### 10 THE PROSTATE ANTIGEN P503S

As described above, P503S is found on the surface of prostate cells. Secondary coated microsphere beads specific for mouse IgG were coupled with the purified P503S-specific monoclonal antibody 1D12. The bound P503S antibody was then used to capture HEK cells expressing recombinant P503S. This provides a model system for prostate-specific cell capture which may be usefully employed in the detection of prostate cells in blood, and therefore in the detection of prostate cancer.

P503S-transfected HEK cells were harvested and redissolved in wash buffer (PBS, 0.1% BSA, 0.6% sodium citrate) at an appropriate volume to give at least  $5^4$  cells per sample. Round bottom Eppendorf tubes were used for all procedures involving beads. The stock concentrations were as shown below in Table VIII.

Table VIII

Stock concentrations	Sample concentration	Amount needed
Epithelial enrich beads $4^8$ beads/ml (DynaL Biotech Inc. Lake Success, NY)	$1^7$ beads/ml	125 ul stock per 5 ml volume
1D12 ascites antibody 2 mg/ml	0.1 ug/ml (0.1X) to 5 ug/ml (5X) titrations	0.05 ul to 2.5 ul stock per sample
$\alpha$ - Mamma Mu 0.9 mg/ml	1 ug/ml (1X)	1.1 ul stock per sample
Pan-mouse IgG beads $4^8$ beads/ml (DynaL Biotech)	$1^7$ beads/ml	125 ul stock per 5 ml volume

Blocked immunomagnetic beads were pre-washed as follows: all beads needed were pooled and washed once with 1 ml wash buffer. The beads were resuspended in a 3X volume of 1% BSA (v/v) in wash buffer and incubated for 15 min rotating at 4 °C. The beads were then washed three times with 2X volume of wash buffer and resuspended to original volume. Non-blocked beads were pooled, washed three times with 2X volume of wash buffer and resuspended to original volume.

Primary antibody was incubated with secondary beads in a fresh Eppendorf for 30 minutes, rotating at 4 °C. Approximately 200 ul wash buffer was added to increase the total volume for even mixing of the sample. The antibody-bead solution was transferred to a fresh Eppendorf, washed twice with an equal volume of wash buffer and resuspended to original volume. Target cells were added to each sample and incubated for 45 minutes, rotating at 4 °C. The tubes were transferred to a magnet, the supernatant removed, taking care not to agitate the beads, and the samples were washed twice with 1 ml wash buffer. The samples were then ready for RT-PCR using a Dynabeads mRNA direct microkit (DynaL Biotech).

Epithelial cell enrichment was placed in a magnet and supernatant was removed. The epithelial enrichment beads were then resuspended in 100 ul lysis/binding buffer fortified with Rnasin (2 U/ul per sample), and stored at -70 °C until use. Oligo (dT<sub>25</sub>) Dynabeads were pre-washed as follows: all beads needed were pooled (23 ul/sample), washed three times with an excess volume of lysis/binding buffer, and resuspended to original volume. The lysis supernatant was separated with a magnet and transferred to a fresh Eppendorf. 20 ul oligo(dT<sub>25</sub>) Dynabeads were added per sample and rolled for 5 min at room temperature. Supernatant was separated using a magnet and discarded, leaving the mRNA annealed to the beads. The bead/mRNA complex was washed with buffer and resuspended in cold Tris-HCl.

For RT-PCR, the Tris-HCl supernatant was separated and discarded using MPS. For each sample containing 1<sup>5</sup> cells or less, the following was added to give a total volume of 30 ul: 14.25 ul H<sub>2</sub>O; 1.5 ul BSA; 6 ul first strand buffer; 0.75 mL 10 mM dNTP mix; 3 ul Rnasin; 3 ul 0.1M dTT; and 1.5 ul Superscript II. The resulting solution was incubated for 1 hour at 42 °C, diluted 1:5 in H<sub>2</sub>O, heated at 80°C for 2 min

to detach cDNA from the beads, and immediately placed on MPS. The supernatant containing cDNA was transferred to a new tube and stored at  $-20^{\circ}\text{C}$ .

Table IX shows the percentage of capture of P503S-transfected HEK cells as determined by RT-PCR.

5

Table IX

	% capture P503S-transfected HEK cells	% capture LnCAP cells
0.1 ug/ml P503S Mab	36.90	0.00
0.5 ug/ml P503S Mab	67.40	2.93
1 ug/ml P503S Mab	40.22	0.00
5 ug/ml P503S Mab	13.11	0.00
Anti-Mu beads only, non-blocked	1.42	0.00
Anti-Mu beads only, blocked	15.65	20.21
Absolute control, non-capture cells	100.00	100.00

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From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

## CLAIMS

## What is Claimed:

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(b) sequences having at least 70% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(c) sequences having at least 90% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(d) sequences encoded by a polynucleotide of claim 1;

(e) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and

(f) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;

(c) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591,

593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 2,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.



13. A method for the treatment of a cancer in a patient, comprising administering to the patient a composition of claim 11.

14. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 8;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

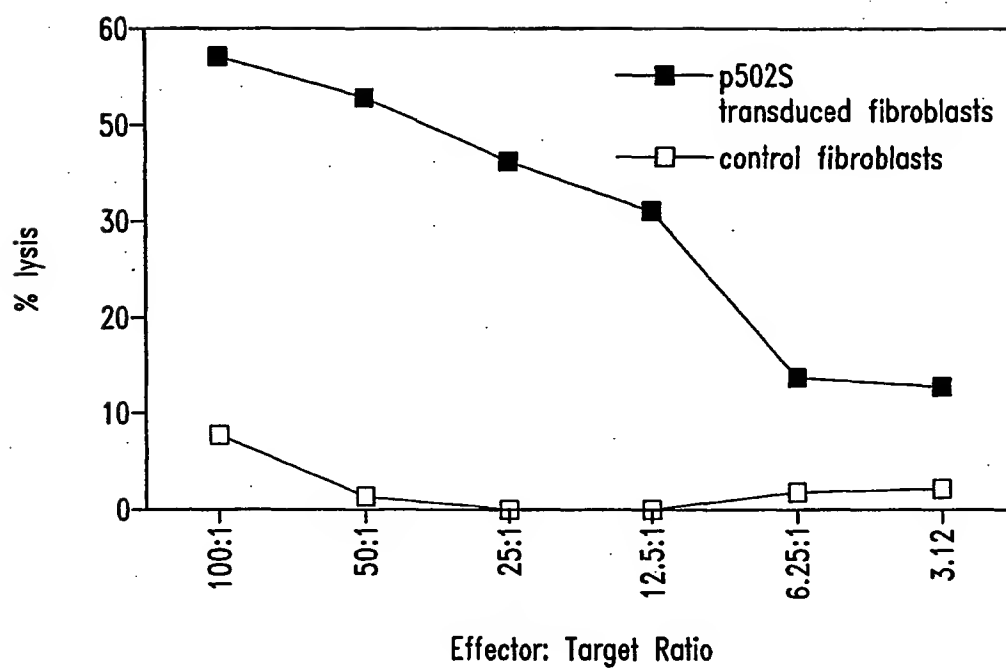
15. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

16. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

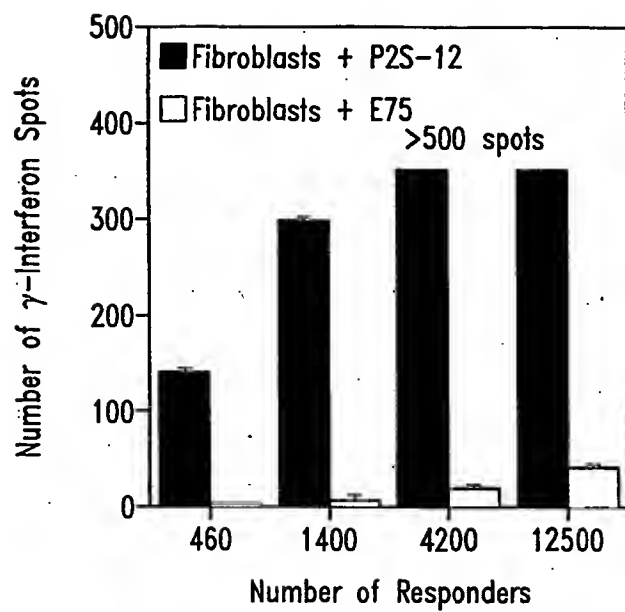
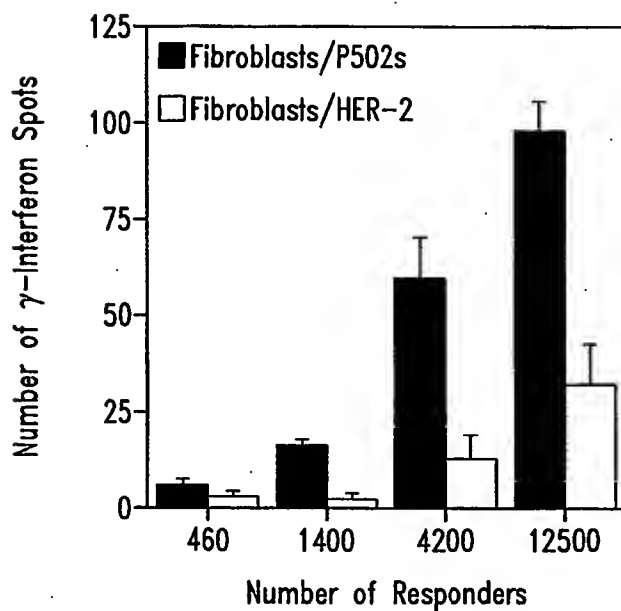
17. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

- (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate;
  - (b) administering to the patient an effective amount of the proliferated T cells,
- and thereby inhibiting the development of a cancer in the patient.

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*Fig. 1*

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*Fig. 2A**Fig. 2B*

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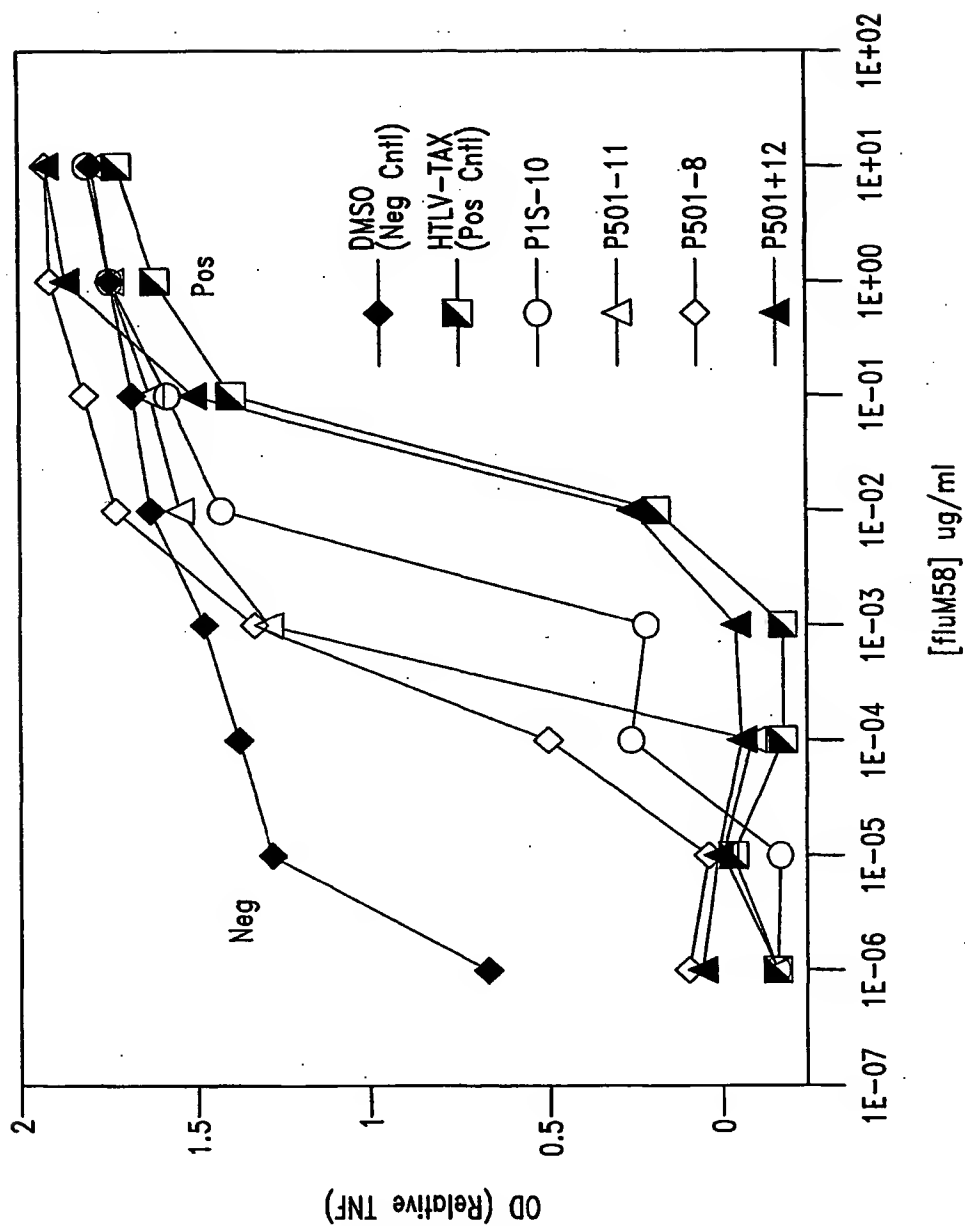
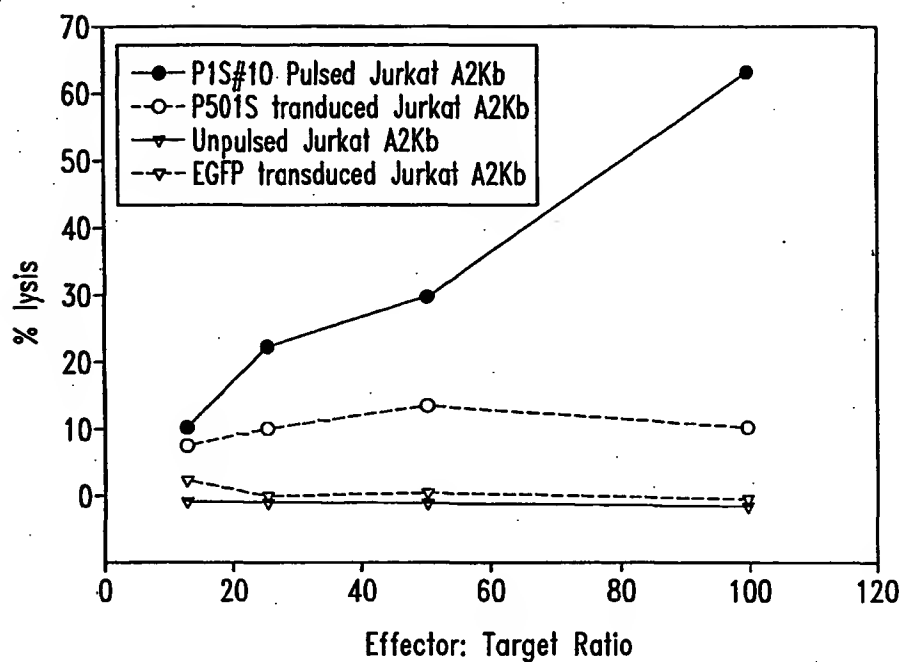
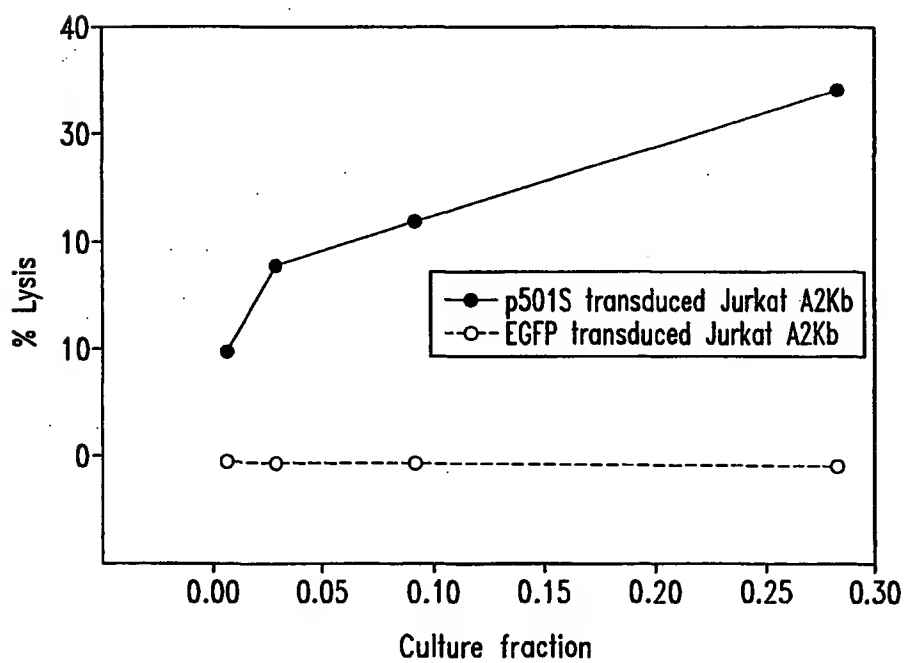
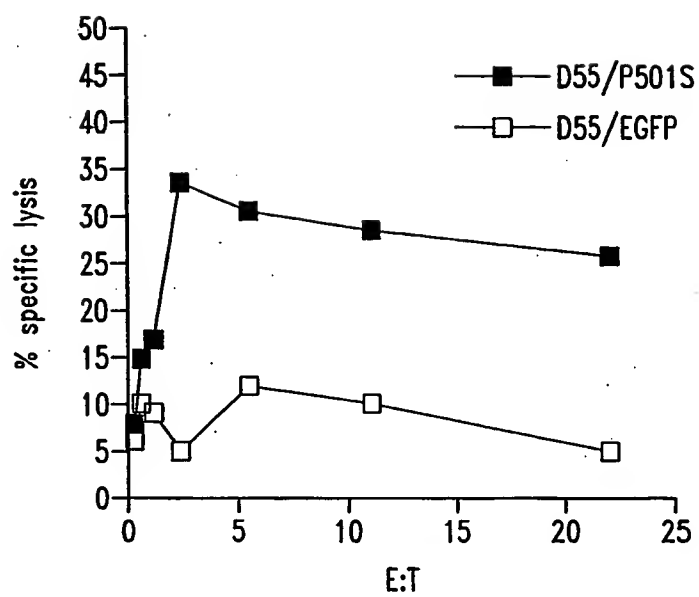
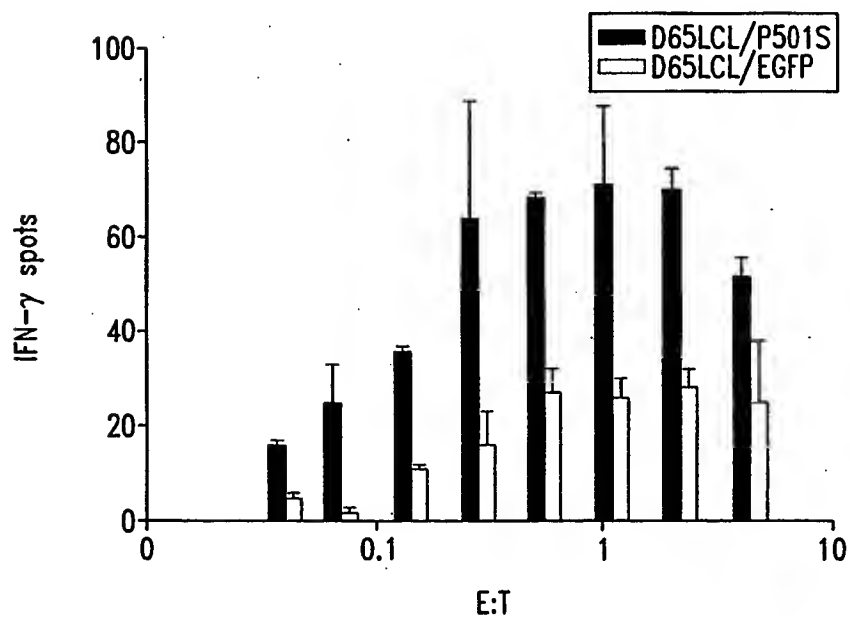


Fig. 3

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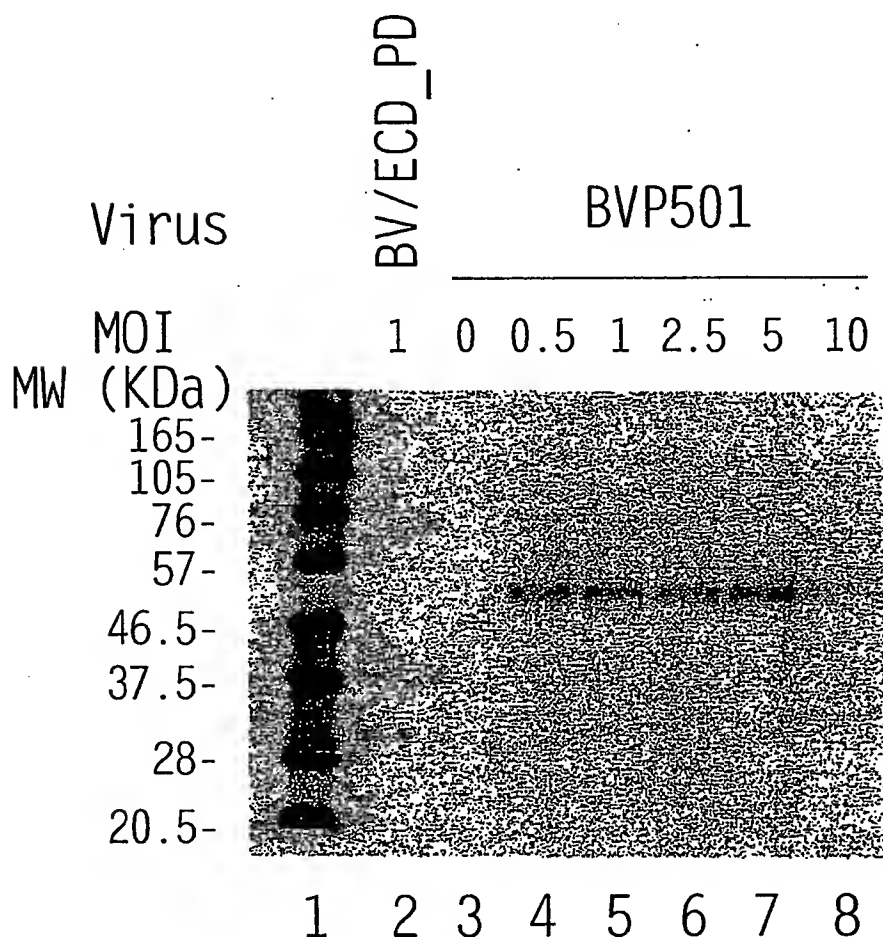
*Fig. 4**Fig. 5*

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*Fig. 6A**Fig. 6B*

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Expression of P501S  
by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD\_PD (lane2), without virus (lane3), or with recombinant baculovirus for P501 at different MOIs (lane 4-8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

*Fig. 7*

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FIGURE 8. Mapping of the epitope recognized by 10E3-G4-D3

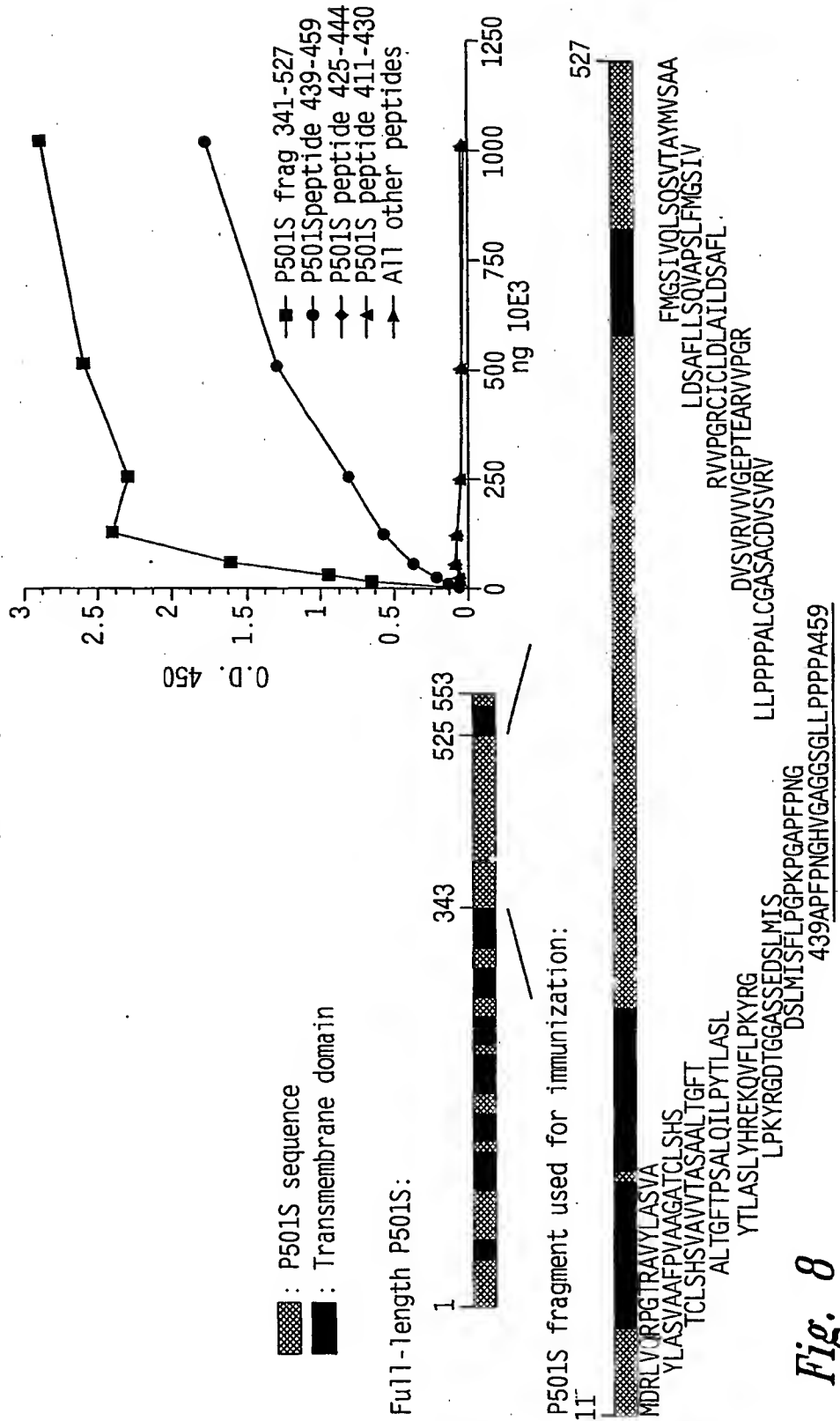


Fig. 8



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Schematic of P501S with predicted  
transmembrane, cytoplasmic, and extracellular regions

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TMVLGIGPVLGLVCYPLLGSAS

*DHWRGRYGRRRP* FIWALSLGILLSLFLIPRAGWL AGLLCPDPRPLE LALLILGVGLLDFCGQVCFTPL  
EALLSDLFRDPDHCRQ AYSVAFMISLGGCLGYLLPAI **DWDTSALAPYLGTQEE**

CLFGLLTLIFLTCVAATLLV AEAAALGPTEPAEGLSAPSLSPHCCPCRARLAFRNLGALLPRL  
HQLCCRMPRTLRR LFVAELCSWMALMTFTLFYTDF VGEGLYQGVPRAPGTEARRHYDEGVR

MGSLGLFLQCAISLVFSLVM DRLVQRFGTRAVYLAS VAAFPVAAGATCLSHSVAVVTA **SAA**

LTGFTFSALQILPYTLASLY **HREKQVFLPKYRGDTGGASSED** SLMTSFLPGPKPGAPFPNGHVAGGSGSL

LPPPPALCGASACDVSVRVVVGEPTARVVPGRG ICDLAILD SAFLLSQVAPSLF **MGSIVQLSQS**

VTAYMVSAAGLGLVAIYFAT QVVF **DKSDLAKYSA**

Underlined sequence: Predicted transmembrane domain; **Bold sequence**:  
 Predicted extracellular domain; *Italic sequence*: Predicted intracellular  
 domain. Sequence in bold/underlined: used generate polyclonal rabbit  
 serum

Localization of domains predicted using HMMP (G.E. Tusnady and I. Simon  
 (1998) Principles Governing Amino Acid Composition of Integral Membrane  
 Proteins: Applications to topology Prediction. J. Mol. Biol. 283, 489-506.

*Fig. 9*

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Genomic Map of (5) Corixa Candidate Genes

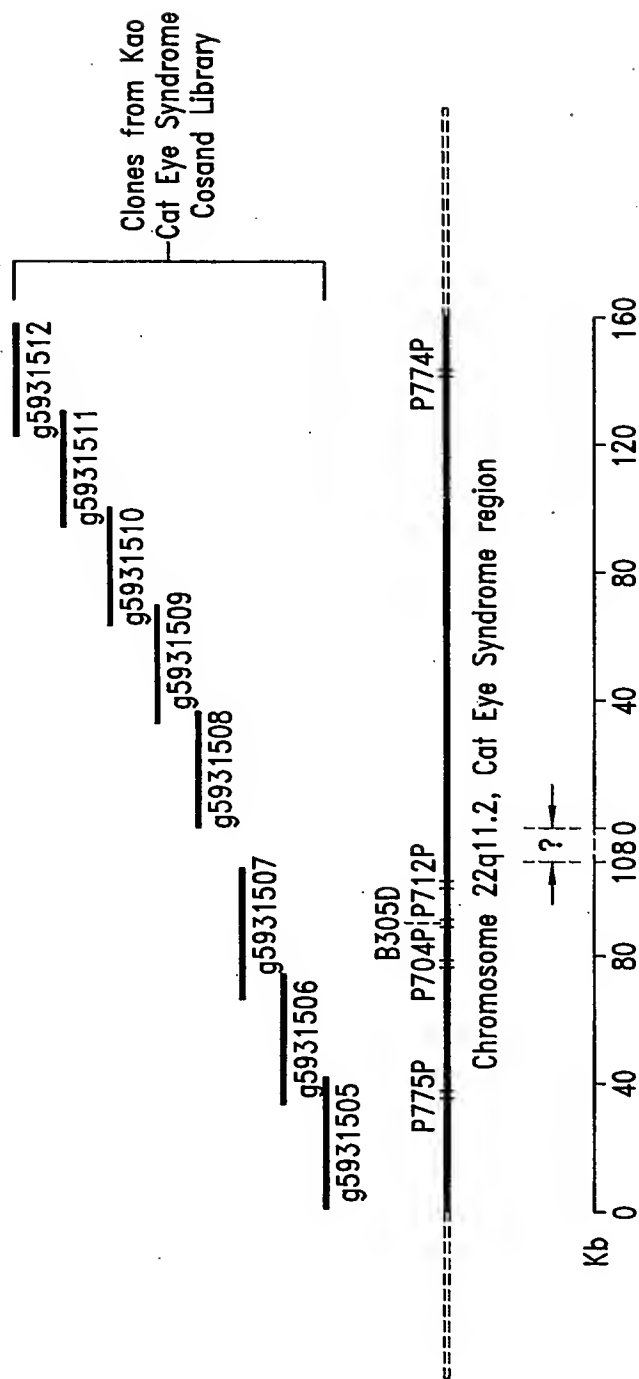


Fig. 10

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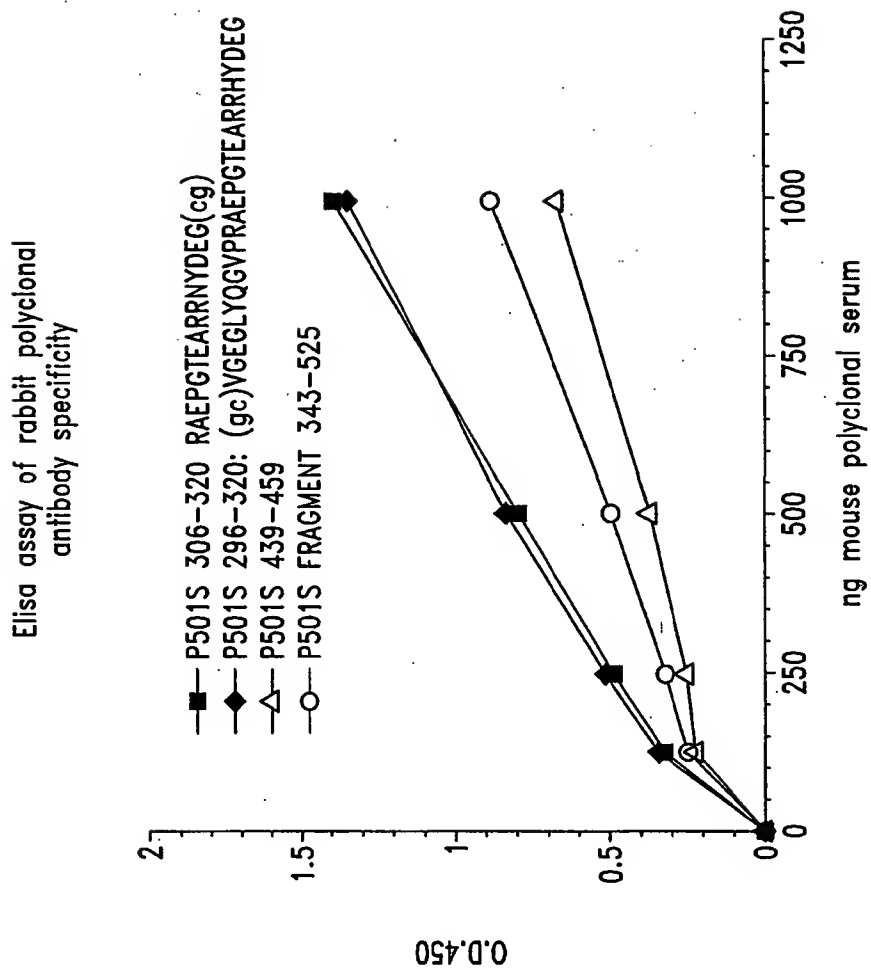


Fig. 11

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```

*Fig. 12A (1)*

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*Fig. 12A (2)*

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*Fig. 12A (3)*

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*Fig. 12B*

## SEQUENCE LISTING

<110> Corixa Corporation  
 Xu, Jiangchun  
 Dillon, Davin C.  
 Mitcham, Jennifer L.  
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 Carter, Darrick  
 Li, Samuel  
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 tccatgtcca tctgattggg aagttcatca gactttagtc canntccttt gatcagcagc 300  
 tcgtagaact ggggttctat tgcctcaaca gccatgaatt ccccatctgc tgcctgtaa 360  
 gtcgtataga aaggtgctcc accatccaac atgttctgtc ctcgaggggg ggcccgggtac 420  
 ccaattcggc ctatantgag tcgtattacg cgcgctcact ggccgtcgtt ttacaacgtc 480  
 gtgactggga aaacctggg cgttaccac ttaatcgctt tgcagcaat ccccttttcg 540  
 ccagctgggc gtaatanca aaaggcccg accgatcgcc cttccaacag ttgcgcacct 600  
 gaatgggnaa atgggacccc cctgttaccg cgcattnaac ccccgcnagg tttngttgtt 660  
 acccccacnt nnaccgctta cactttgcca ggcgcttanc gcccgctccc tttcnccttt 720  
 cttcccttcc tttcncncn ctttccccg ggggttcccc cntcaaacc cna 773

<210> 4  
 <211> 828  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(828)  
 <223> n = A,T,C or G

<400> 4

cctcctgagt	cctactgacc	tgtgctttct	ggtgtggagt	ccagggctgc	taggaaaagg	60
aatgggcaga	cacaggtgta	tgccaatggt	tctgaaatgg	gtataatttc	gtcctctcct	120
tcggaacact	ggctgtctct	gaagacttct	cgctcagttt	cagtgaggac	acacacaaaag	180
acgtgggtga	ccatgttggt	tgtgggggtgc	agagatggga	gggggtgggc	ccaccctgga	240
agagtggaca	gtgacacaag	gtggacactc	tctacagatc	actgaggata	agctggagcc	300
acaatgcatg	aggcacacac	acagcaagga	tgaacnctgta	aacatagccc	acgctgtcct	360
gngggcactg	ggaagcctan	atnaggccgt	gagcanaaag	aaggggagga	tccactagtt	420
ctanagcggc	cgccaccgcg	gtgganctcc	ancttttggt	cccttttagtg	agggttaatt	480
gcgcgcttgg	ontaatcatg	gtcatanctn	tttctgtgtg	gaaattgtta	tccgctcaca	540
attccacaca	acatacganc	cggaacacata	aantgtaaac	ctgggggtgcc	taatgantga	600
ctaactcaca	ttaattgcgt	tgcgtcactc	gcccgccttc	caatcnggaa	acctgtcttg	660
ccncttgcat	tnatgaatcn	gccaaacccc	ggggaaaagc	gtttgcgttt	tgggcgctct	720
tccgcttcct	cnctcantta	ntccctncnc	tcgggtcattc	cggtgcngc	aaaccggttc	780
accncctcca	aagggggtat	tccggtttcc	ccnaatccgg	gghanancc		828

<210> 5  
 <211> 834  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(834)  
 <223> n = A,T,C or G

<400> 5

tttttttttt	tttttactga	tagatggaat	ttattaagct	tttcacatgt	gatagcacat	60
agtttttaatt	gcattccaaag	tactaacaata	aactctagca	atcaagaatg	gcagcatggt	120
atttttataac	aatcaacacc	tgtggctttt	aaaatttgggt	tttcataaga	taattttatac	180
tgaagtaaat	ctagccatgc	ttttaaaaaa	tgcttttaggt	cactccaagc	ttggcagttta	240
acatttggga	taaacaataa	taaaacaatc	acaattttaat	aaataacaaa	tacaacattg	300
taggccataa	tcatatacag	tataaggaaa	agggtgtagt	gttgagtaag	cagttattag	360
aatagaatac	cttggcctct	atgcaaatat	gtctagacac	tttgattcac	tcagccctga	420
cattcagttt	tcaaagtagg	agacagggttc	tacagtatca	ttttacagtt	tccaacacat	480
tgaaaaacaag	tagaaaatga	tgagttgatt	tttattaatg	cattacatcc	tcaagagtta	540
tcaccaaccc	ctcagttata	aaaaattttc	aagttatatt	agtcataata	cttgggtgtgc	600
ttatttttaa	ttagtgtctaa	atggattaaag	tgaagacaac	aatgggtcccc	taatgtgatt	660
gatattggtc	atttttacca	gcttctaaat	ctnaactttc	aggcttttga	actggaacat	720
tgnatnacag	tgttccanag	ttncacaccta	ctggaacatt	acagtgtgct	tgattcaaaa	780
tgttattttt	ttaaaaatta	aatttttaacc	tggtggaaaa	ataatttgaa	atna	834

<210> 6  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(818)  
 <223> n = A,T,C or G

<400> 6

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tttttttttt tttttttttt aagaccctca tcaatagatg gagacataca gaaatagtca      60
aaccacatct acaaaatgcc agtatcaggg ggcggttcg aagccaaagt gatgtttgga      120
tgtaaagtga aatattagtt ggcggatgaa gcagatagtg aggaaagttg agccaataat      180
gacgtgaagt ccgtggaagc ctgtggctac aaaaaatgtt gagccgtaga tgccgtcgga      240
aatggtgaag ggagactcga agtactctga ggctttagg agggtaaaat agagaccag      300
taaaattgta ataagcagtg cttgaattat ttggtttcgg ttgttttcta ttagactatg      360
gtgagctcag gtgattgata ctctgatgc gagtaatacg gatgtgttta ggagtgggac      420
ttctagggga tttagcgggg tgatgcctgt tggggggccag tggcctccta gttggggggg      480
aggggctagg ctggagtggg aaaaggctca gaaaaatcct gcgaagaaaa aaacttctga      540
ggtataaat aggattatcc cgtatcgaa gcctttttgg acaggtgggtg tgtgtgggcc      600
ttggtatgtg ctttctcgtg ttacatcgcg ccatcattgg tatatggtta gtgtgtggg      660
ttantangcg ctantatgaa gaacttttgg antggaatta aatcaatngc ttggccggaa      720
gtcattanga nggctnaaaa ggccctgtta ngggtctggg ctnggtttta cccnaccat      780
ggaatncncc ccccggaacna ntgnatccct attcttaa      818

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```

<210> 7
<211> 817
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(817)
<223> n = A,T,C or G

```

```

<400> 7
tttttttttt tttttttttt tggctctaga gggggtagag ggggtgctat agggtaaata      60
cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt      120
ggtttgctcc acagatttca gagcattgac cgtagtatac ccccggtcgt gtagcgggtga      180
aagtgttttg gtttagacgt ccgggaattg catctgtttt taagcctaata gtggggacag      240
ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcgagg      300
gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg      360
gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc      420
attggtggcc aattgatttg atggttaagg gagggatcgt tgaactcgtc tgttatgtaa      480
aggatncctt ngggatggga aggcnatnaa ggactangga tnaatggcgg gcangatatt      540
tcaaacngtc tctanttcct gaaacgtctg aaatgttaat aanaattaan tttngttatt      600
gaatntnnng gaaaagggct tacaggacta gaaaccaaata angaaaanta atnntaangg      660
cnttatcntn aaaggtnata accnctccta tnatcccacc caatngnatt cccacnccn      720
acnattggat nccccanttc canaaanggc cccccccggt tgnannccnc cttttgttcc      780
cttnantgan ggttattcnc ccctngcntt atcancc      817

```

```

<210> 8
<211> 799
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G

```

```

<400> 8
catttcgggg tttactttct aaggaaagcc gagcgggaagc tgctaacgtg ggaatcggtg      60
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt      120
ctgaagcgca cgtcccagaa ggtggacttg gcactgaaac agctgggaca catccgcgag      180
tacgaacagc gcctgaaagt gctggagcgg gaggtccagc agtgtagccg cgtcctgggg      240
tggttgcccg angcctganc cgctctgcct tgctgcccc angtgggccg ccacccctg      300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac cccacangg      360

```

ggatTTTgct	cctanantaa	ggctcatctg	ggcctcggcc	ccccacctg	gttggccttg	420
tctttgangt	gagcccatg	tccatctggg	ccactgtcng	gaccaccttt	ngggagtgtt	480
ctccttacaa	ccacannatg	cccggtcctt	cccggaacc	antccancc	tgngaaggat	540
caagnctgn	atccactnnt	nctanaaccg	gccnccnccg	cngtggaacc	cnccttntgt	600
tccttttctt	tnagggttaa	tnnccgcttg	gccttnccan	ngtcctnccn	nttttccnnt	660
gttnaaattg	ttangcnccc	nccnntcccn	cnnccnccan	cccgaccenn	annntnnann	720
ncctgggggt	ncnncngat	tgaccenncc	nccctntant	tgcnttnggg	nncnntgccc	780
ctttccctct	nggganncg					799

&lt;210&gt; 9

&lt;211&gt; 801

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(801)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 9

acgccttgat	cctcccaggc	tgggactggt	tctgggagga	gccgggcatg	ctgtggtttg	60
taangatgac	actcccaaag	gtggctcctga	cagtggccca	gatggacatg	gggctcacct	120
caaggacaag	gccaccagg	gcgggggccc	aagcccatat	gatccttact	ctatgagcaa	180
aatcccctgt	gggggcttct	ccttgaagtc	cgccancagg	gctcagtctt	tggaccctang	240
cagggtcatg	ggttgtngnc	caactggggg	ccncaacgca	aaanggcna	gggcctcngn	300
cacccatccc	angacggggc	tacactnctg	gacctccnc	tccaccactt	tcatgcgctg	360
ttcntaccgc	cgnatntgtc	ccanctgttt	cngtgccnac	tccancttct	nggacgtgcg	420
ctacatacgc	ceggantcnc	netcccgttt	tgctccctatc	cacgtncan	caacaaattt	480
cncctantg	caccnattcc	caenttttnc	agntttccnc	nncgngcttc	cttntaaaag	540
ggttganccc	cggaaaatnc	cccaaagggg	gggggcccng	taccaactn	ccccctnata	600
gctgaantcc	ccatnaccnn	gnctcnatgg	ancntccnt	ttaannacn	ttctnaactt	660
gggaanancc	ctcgnccntn	ccccnttaa	tccncccttg	cnangnncnt	cccccnntcc	720
ncccnntng	gcntntnann	cnaaaaggc	ccnnancaa	tctcctnncn	cctcanttgc	780
ccanccctcg	aatcggccn	c				801

&lt;210&gt; 10

&lt;211&gt; 789

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(789)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 10

cagtctatnt	ggccagtgtg	gcagctttcc	ctgtggctgc	cggtgccaca	tgctgtccc	60
acagtgtggc	cgtggtgaca	gcttcagccg	ccctcaccgg	gttcaccttc	tcagccctgc	120
agatcctgcc	ctacacactg	gcctccctct	accaccggga	gaagcagggt	ttcctgccc	180
aataccgagg	ggacactgga	ggtgctagca	gtgaggacag	cctgatgacc	agcttcctgc	240
caggccctaa	gcttgagct	ccctcccta	atggacacgt	gggtgctgga	ggcagtggcc	300
tgctcccacc	tccaccgcg	ctctcgggg	cctctgcctg	tgatgtctcc	gtacgtgtgg	360
tggtgggtga	gcccaccgan	gccagggtgg	ttccggggcg	gggcatctgc	ctggacctgc	420
ccatcctgga	tagtgcttcc	tgctgtccca	ngtggcccca	tccctgttta	tgggtccat	480
tgtccagctc	agccagtctg	tcactgccta	tatgtgtctt	gccgcaggcc	tgggtctggt	540
cccatttact	ttgctacaca	ggtantattt	gacaagaacg	anttggccaa	atactcagcg	600
ttaaaaaatt	ccagcaacat	tgggggtgga	aggcctgcct	cactgggtcc	aactccccgc	660
tcctgttaac	cccatggggc	tgccggcttg	gccgccaat	tctgttgctg	ccaaantnat	720

gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct ngggggggtng 780  
 gpggttccc 789

<210> 11

<211> 772

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(772)

<223> n = A,T,C or G

<400> 11

ccccacctac	ccaaatatta	gacaccaaca	cagaaaagct	agcaatggat	tcctttctac	60
tttggttaaat	aaataagtta	aatatttaaa	tgccctgtgc	tctgtgatgg	caacagaagg	120
accaacaggc	cacatcctga	taaaaggtaa	gaggggggtg	gatcagcaaa	aagacagtgc	180
tgtgggctga	ggggacctgg	ttcttgtgtg	ttgcccctca	ggactcttcc	cctacaaata	240
actttcatat	gttcaaatac	catggaggag	tgtttcatcc	tagaaactcc	catgcaagag	300
ctacattaaa	cgaagctgca	ggttaagggg	cttanagatg	ggaaccagg	tgactgagtt	360
tattcagctc	ccaaaaaccc	ttctctaggt	gtgtctcaac	taggaggcta	gctgttaacc	420
ctgagcctgg	gtaatccacc	tcagaggtcc	ccgcattcca	gtgcatggaa	cccttctggc	480
ctccctgtat	aagtcagac	tgaaaccccc	ttggaaggnc	tccagtcagg	cagccctana	540
aactggggaa	aaaagaaaag	gacgccccan	ccccagctg	tgcanctacg	cacctcaaca	600
gcacaggggtg	gcagcaaaaa	aaccacttta	ctttggcaca	aacaaaaact	ngggggggca	660
accccggcac	cccnangggg	gttaacagga	ancngggnaa	cntggaaccc	aattnaggca	720
ggcccnccac	ccnnaatntt	gctgggaaat	ttttctctcc	ctaaattntt	tc	772

<210> 12

<211> 751

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(751)

<223> n = A,T,C or G

<400> 12

gccccaatte	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatataaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcttgg	gcaggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
aagtanggtg	agtccctcaaa	atccgtatag	ttggtgaagc	cacagcactt	gagccctttc	240
atggtggtgt	tccacacttg	agtgaagtct	tcctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	ggaagtgtc	agccattgtg	gtgtacacca	aggcgaccac	360
agcagctgcn	acctcagcaa	tgaagatgan	gaggangatg	aagaagaacg	tcncgagggc	420
acacttgctc	tcagtcttan	caccatanca	gcccntgaaa	accanana	aagaccacna	480
cnccggctgc	gatgaagaaa	tnaccccneg	ttgacaaact	tgcatggcac	tggganccac	540
agtggccnna	aaaatcttca	aaaaggatgc	cccatcnatt	gaccccccaa	atgcccactg	600
ccaacagggg	ctgccccacn	cncnnaacga	tgancnatt	gnacaagatc	tncntggtct	660
tnatnaacnt	gaaccctgcn	tngtggctcc	tgttcaggnc	cnnggcctga	cttctnaann	720
aangaactcn	gaagncccca	cngganannc	g			751

<210> 13

<211> 729

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(729)  
 <223> n = A,T,C or G

<400> 13  
 gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgcctt 60  
 tgtggancct cagcagtncc ctctttcaga actcantgcc aagancctg aacaggagcc 120  
 accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gtcacatctt 180  
 ctgtgtggty cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcacccctt 240  
 ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300  
 ctcatcgag ccggcgttgt ggtcttagct ctagggttcc tgggctgcta tgggtgctaag 360  
 actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct 420  
 gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt 480  
 tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaaanact tcaactcaagt 540  
 gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt 600  
 gaagantcac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa 660  
 acgtccccaa cacagccaat tgaaaacctg caccacaacc aaanggggtc ccaaccanaa 720  
 attnaaggg 729

<210> 14  
 <211> 816  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(816)  
 <223> n = A,T,C or G

<400> 14  
 tgctcttcct caaagtgtt cttgttgcca taacaaccac cataggtaaa gcgggagcag 60  
 tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgacagag tcctgtgtct 120  
 ggcaggtcca cgcagtgcc tttgtcactg gggaaatgga tgcgctggag ctgctcaaag 180  
 cactcgtgt attttcaca ggcagcctcg tccgacgcgt cggggcagtt gggggtgtct 240  
 tcacactcca ggaactgtc natgcagcag ccattgctgc agcggaaactg ggtgggctga 300  
 cangtgccag agcacactgg atggcgctt tccatgnnan gggccctgng ggaaagtccc 360  
 tganccccc anctgcctct caaangcccc accttgaca ccccgacagg ctagaatgga 420  
 atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt 480  
 gcanatctgc tccnggggg tcntantacc ancgtgggaa aagaaccca ggcngcgaac 540  
 caancttgtt tggatncaa gcnataatct nctnttctgc ttggtggaca gcaccantna 600  
 ctgtnnanct ttagnccntg gtcctcntgg gttgnncttg aacctaatcn ccnntcaact 660  
 gggacaaggt aantngccnt cctttnaatt ccnancntn cccctggtt tggggttttn 720  
 cncnctcta ccccgaaaa nccgtgttcc ccccaacta ggggcnaaa ccnntnttc 780  
 cacaacctn cccacccac gggttcngnt ggttng 816

<210> 15  
 <211> 783  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(783)  
 <223> n = A,T,C or G

<400> 15  
 ccaaggcctg ggcaggcata nacttgaagg tacaaccca ggaacccctg gtgctgaagg 60

atgtggaaaa	cacagattgg	cgctactgc	gggtgacac	ggatgtcagg	gtagagagga	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaang	cacctacctg	ttccagctga	180
cagtgtactag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtcaact	gtgtgtgtcca	240
ccaagcagac	agaagactac	tgctctgcat	ccaacaangt	gggtcgctgc	cggggctctt	300
tcccacgctg	gtactatgac	cccacggagc	agatctgcaa	gagtttcgtt	tatggaggct	360
gcttggggcaa	caagaacaac	taccttcggg	aagaagagtg	cattctancc	tgtcnggggtg	420
tgcaaggtgg	gcctttgana	ngcanctctg	gggtcangc	gactttcccc	cagggccccct	480
ccatggaaag	gcgccatcca	ntgttctctg	gcacctgtca	gcccaccag	ttccgtgtgca	540
ncaatggctg	ctgcatcnac	antttcctng	aattgtgaca	acacccccca	ntgcccccaa	600
ccctcccaac	aaagcttccc	tgttnaaaaa	tacnccantt	ggcttttnac	aaacnccccg	660
cncctccntt	ttccccnntn	aacaaagggc	nctngcnttt	gaactgccn	aaccnnggaa	720
tctnccnngg	aaaaantncc	ccccctgggt	cctnnaancc	cctccncnaa	anctncccc	780
ccc						783

&lt;210&gt; 16

&lt;211&gt; 801

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(801)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 16

gcccccaattc	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatacaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcttggt	gcaggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
aagtaggggtg	agtcctcaaa	atccgtatag	ttggtgaagc	cacagcactt	gagccctttc	240
atggtgggtg	tccacacttg	agtgaagtct	tcctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	gaagtgtca	gccattgttg	tgtacaccaa	ggcgaccaca	360
gcagctgcaa	cctcagcaat	gaagatgagg	aggaggatga	agaagaacgt	cncgagggca	420
cacttgctct	ccgtcttagc	accatagcag	cccangaaac	caagagcaaa	gaccacaacg	480
cnngctgcga	atgaaagaaa	ntaccacagt	tgacaaactg	catggccact	ggacgacagt	540
tgccccgaan	atcttcagaa	aagggatgcc	ccatcgattg	aacaccana	tgcccactgc	600
cnacagggct	gcnccnncn	gaaagaatga	gccattgaag	aaggatcnc	ntggtcttaa	660
tgaactgaaa	cntgtcatgg	tggcccctgt	tcagggctct	tggcagtga	ttctgaaaaa	720
aaggaacngc	nntagccccc	ccaaangana	aaacaccccc	gggtgttgcc	ctgaattggc	780
ggccaaggan	ccctgccccn	g				801

&lt;210&gt; 17

&lt;211&gt; 740

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(740)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 17

gtgagagcca	ggcgtccctc	tgctgccc	ctcagtggca	acacccggga	gctgttttgt	60
cctttgtgga	gcctcagcag	ttccctcttt	cagaactcac	tgccaagagc	cctgaacagg	120
agccaccatg	cagtgtctca	gcttcattaa	gaccatgatg	atcctcttca	atttgctcat	180
ctttctgtgt	ggtgcagccc	tgttggcagt	gggcatctgg	gtgtcaatcg	atggggcatc	240
ctttctgaag	atcttcgggc	cactgtcgtc	cagtgccatg	cagtttgtca	acgtgggcta	300
cttctcatc	gcagccggcg	ttgtggtctt	tgtcttgggt	ttcctgggct	gctatgggtg	360
taagacggag	agcaagtgtg	ccctcgtgac	gttcttcttc	atcctcctcc	tcattctcat	420

tgctgaagtt	gcagctgctg	tggtcgccctt	ggtgtacacc	acaatggctg	aaccattcct	480
gacgttgctg	gtantgcctg	ccatcaanaa	agattatggg	ttcccaggaa	aaattcactc	540
aantntggaa	caccnccatg	aaaagggctc	caatttctgn	tggttcccc	aactataccg	600
gaatthtgaa	agantcnccc	tacttccaaa	aaaaaanant	tgcttttnc	cccnttctgt	660
tgcaatgaaa	acntcccaan	acngccaatn	aaaacctgcc	cnnncaaaaa	ggntcncaaa	720
caaaaaaant	nnaagggttn					740

&lt;210&gt; 18

&lt;211&gt; 802

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(802)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 18

ccgctgggtg	cgctgggtcca	gngnagccac	gaagcacgtc	agcatacaca	gcctcaatca	60
caaggtcttc	cagctgccgc	acattacgca	gggcaagagc	ctccagcaac	actgcatatg	120
ggatacactt	tactttagca	gccagggtga	caactgagag	gtgtcgaagc	ttattcttct	180
gagcctctgt	tagtgaggga	agattccggg	cttcagctaa	gtagtcagcg	tatgtcccat	240
aagcaaacac	tgtgagcagc	cggaaggtag	aggcaaagtc	actctcagcc	agctctctaa	300
cattgggcat	gtccagcagt	tctccaaaca	cgtagacacc	agnggcctcc	agcacctgat	360
ggatgagtgt	ggccagcgct	gcccccttgg	ccgacttggc	taggagcaga	aattgctcct	420
ggttctgccc	tgctaccttc	acttccgcac	tcactactgc	actgagtgtg	ggggacttgg	480
gctcaggatg	tccagagacg	tggttccgcc	ccctcnctta	atgacaccgn	ccanncaacc	540
gtcggctccc	gccgantgng	ttcgtcgtnc	ctgggtcagg	gtctgctggc	cnctacttgc	600
aanccttcgtc	nggcccatgg	aattcaccnc	accggaactn	gtangatcca	ctnnttctat	660
aaccggncgc	caccgcnnnt	ggaactccac	tcttnttnc	tttacttgag	ggttaagggtc	720
acccttnncg	ttaccttggt	ccaaaccntn	ccntgtgtcg	anatngtnaa	tcnggnccna	780
tnccancnc	atangaagcc	ng				802

&lt;210&gt; 19

&lt;211&gt; 731

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(731)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 19

cnaagcttcc	aggtnacggg	ccgcnaancc	tgaccnagg	tancanaang	cagnncgagg	60
gagcccaccg	tcacgngngg	nggtctttat	nggagggggc	ggagccacat	cnctggacnt	120
cntgacccca	actcccncc	ncncantgca	gtgatgagtg	cagaactgaa	ggtnacgtgg	180
caggaaccaa	gancaaannc	tgctccnntc	caagtcggcn	nagggggcgg	ggctggccac	240
gcncatcent	cnagtgtctg	aaagcccn	cctgtctact	tgtttgaga	acngcnnga	300
catgcccagn	gttanataac	nggcngagag	tnantttgcc	tctcccttcc	ggctgcgc	360
cgngtntgct	tagnggacat	aacctgacta	cttaactgaa	ccnngaatac	tnccnccct	420
ccactaagct	cagaacaaaa	aacttcgaca	ccactcantt	gtcacctgnc	tgctcaagta	480
aagtgtaccc	catncccaat	gtntgctnga	ngctctgncc	tgcnttangt	tcggtcctgg	540
gaagacctat	caattnaagc	tatgtttctg	actgcctctt	gtccctgna	acaancnacc	600
cnnnntcca	agggggggnc	ggcccccaat	ccccccaacc	ntnaattnan	tttancccn	660
ccccngggc	cggcctttta	cnancntcnn	nnaacnggna	aaaccnnngc	tttncccaac	720
nnaatccncc	t					731



<210> 20  
 <211> 754  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(754)  
 <223> n = A,T,C or G

<400> 20  
 tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60  
 caaccccctc ntccaaatnn ccttttccgg gnggggggttc caaacccaan ttannnttgg 120  
 annntaaatt aaatnttntt tggngggnna anccnaatgt nangaaagtt naaccanta 180  
 tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240  
 aaatngttna nggaaaaccc aatttctcnt aaggttggtt gaaggntnaa tnaaaanccc 300  
 nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360  
 ggnnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg 420  
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntccggg 480  
 ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc 540  
 ccagngtgag nntnggggtt nccccccccc canggccct ctcgnanagt tggggtttgg 600  
 ggggcctggg attttntttc cctnttnc tccccccccc ccnggganag aggttngngt 660  
 tttgntcnnc ggcccnccn aagantttt ccganttnan ttaaatcctt gcctnggcga 720  
 agtccnttgn agggntaaan ggccccctnn cggg 754

<210> 21  
 <211> 755  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(755)  
 <223> n = A,T,C or G

<400> 21  
 atcancccat gaccnnaac nngggaccnc tcancggnc nnncnaccnc cggccnatca 60  
 nngtnagnnc actncnnttn natcacnccc cnccnactac gcccnananc cnacgcncta 120  
 nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180  
 ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattt 240  
 nncnncanat gattttcctn anccgattac cctncccccc tanccctcc cccccaacna 300  
 cgaaggcnct ggnccnaagg nngcgnccc ccgctagntc cccnncaggt cncnnccta 360  
 aactcancn nattaacncc ttcttgagta tcactccccg aatctcacc tactcaactc 420  
 aaaaanactn gatacaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480  
 ttagnggtcc ntnaancntc ctaatacttc cagtctnctc tcnccaattt ccnaanggct 540  
 ctttcngaca gcatnttttt gtccccnntt gggttcttan ngaattgcc ttctntgaac 600  
 gggctctctt tttccttcgg ttancctggg ttcnncgggc cagttattat ttccntttt 660  
 aaattctncc cntttanttt tggentttna aacccccggc cttgaaaacg gccccctggt 720  
 aaaaggttgt tttganaaaa tttttgtttt gtccc 755

<210> 22  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(849)

<223> n = A,T,C or G

<400> 22

tttttttttt	tttttangtg	tngtcgtgca	ggtagaggct	tactacaant	gtgaanacgt	60
acgctnggan	taangcgacc	cgantttctag	gannncncct	aaaatcanac	tgtgaagatn	120
atcctgnnna	cggaanggtc	accggnngat	nntgctaggg	tgncncctcc	cannncnttn	180
cataactcng	nggccctgcc	caccaccttc	ggcggcceng	ngnccgggcc	cggttcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	nccccnncng	accnnggcga	tccggggtn	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccgnccc	ctttaccct	nnacaagcca	360
cngccntcta	nccnngcccc	ccccctccant	nngggggact	gccnanngct	ccgttntctng	420
nnaccccnnn	gggtncctcg	gttgcgcant	cnaaccgnang	ccanggatc	cnaaggaagg	480
tgcgttnttg	gccctaccc	ttcgtctnccg	nnacaccttc	ccgacnanga	nccgtcccg	540
cncnncgng	cctcncctcg	caacacccgc	nctcctcngt	ncggnnnccc	ccccacccgc	600
nccctcncnc	ngnccnancn	ctcncncnc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggngacnng	nagcncnntc	gcncgcgcgn	gcgncncct	cgccncngaa	720
ctnctcngg	ccantnncgc	tcaancnna	cnaaacgccg	ctgcgcggcc	cgnagcgncc	780
nctccncca	gtcctcccg	cttcnacc	angnttccn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(872)

<223> n = A,T,C or G

<400> 23

gogcaaaacta	tacttcgctc	gnactcgtgc	gcctcgtctnc	tcttttctc	cgcaaccatg	60
tctgacnanc	ccgattnggc	ngatatanan	aagntcganc	agtccaaact	gantaacaca	120
cacacncnan	aganaaatcc	nctgccttcc	anagtanaen	attgaacnng	agaaccangc	180
nggggaatcg	taatnaggcg	tgcgcgcga	atntgtcnc	gtttattntn	ccagcctcnc	240
ctnccnacc	tacntcttcn	nagctgtcnn	accctngtn	cgnaccccc	naggtcggga	300
tccgggtttn	nntgaccgng	cnnccctcc	ccccctccat	nacganccnc	ccgcaccacc	360
nanngcncgc	nccecgnnct	cttcgcncnc	ctgtcctntn	ccctgtngc	ctggcncngn	420
acgcattga	ccctcgccnn	ctnccngaaa	ncgnanacgt	ccgggttggn	annancgctg	480
tgggnnngcg	tctgcncgc	gttccttccn	ncnncctcca	ccatcttct	tacnnggtct	540
ccnccgcctc	tcnncacnc	cctgggacgc	tntcctntgc	cccccttnac	tccccctt	600
cgncgtgnc	cgccccacc	ntcatttnca	nacgntcttc	acaannncct	ggntnnctcc	660
cnancngncn	gtcanccnag	ggaaggngg	ggnnccnntg	nttgacgttg	ngngangtc	720
cgaanantcc	tcnccntcan	cncctaccct	cgggcggnct	ctcngttnc	aacttancaa	780
ntctcccccg	ngngcncctc	tcagcctcnc	ccncccnct	ctctgcantg	tnctctgctc	840
tnaccnntac	gantnttcgn	cncctcttt	cc			872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

gcatgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcantaat	catggtcnta	60
------------	------------	------------	------------	-------------	------------	----

## 12

nctgncttcc	tgtgtcaa	gtatacna	tanatatg	tctnatntga	caaganngta	120
tctntcatta	gtaacaantg	tnntgtccat	cctgtcngan	canattccca	tnnattncgn	180
cgcattnccn	gcncantatn	taatngggaa	ntcnntnnn	ncaccnncat	ctatcctncc	240
gcncctgac	tgganagagat	ggatnanttc	tnntntgacc	nacatgttca	tcttggtatn	300
aanancctcc	cgcngnccac	cggttngnng	cnagccnntc	ccaagacctc	ctgtggaggt	360
aacctgcgtc	aganncatca	aacntgggaa	accgcnncc	angtnnaagt	ngnnncanan	420
gateccgtcc	aggnttnacc	atcccttcnc	agcgccccct	ttngtgcctt	anagngnagc	480
gtgtccnanc	cnetcaacat	ganacgcgcc	agncanccg	caattnggca	caatgtcgnc	540
gaacccctta	gggggantna	tncaaanccc	caggattgtc	cncncangaa	atcccnanc	600
ccnccctac	ccncttttg	gacngtgacc	aantcccga	gtncaggtcc	ggcngnctc	660
ccccaccgt	nnccntggg	gggtgaanct	cngntcanc	cngncgaggn	ntcnaagga	720
accggncctn	ggncgaanng	ancnntcnga	agnccnct	ogtataacc	cccctcncca	780
nccnacngnt	agntcccccc	cngggtncgg	aangg			815

&lt;210&gt; 25

&lt;211&gt; 775

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(775)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

ccgagatgtc	tgcctccgtg	gccttagctg	tgctgcgct	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaattt	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgtact	180
tactgaagaa	tgganagaga	attgaaaaag	tggagcattc	agacttgtct	ttcagcaagg	240
actggtcttt	ctatctontg	tactacactg	aattcaccoc	cactgaaaaa	gatgagtatg	300
cctgcccgtg	gaaccatgtg	actttgtcac	agcccaagat	agttaagtgg	gatcgagaca	360
tgtaagcagn	cnnocatgga	gtttgaagat	gcgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcnttttaat	antgatatgc	ntatacaccc	taccctttat	gnccccaat	480
tgtaggggtt	acatnantgt	tcnctnngga	catgatcttc	ctttataant	ccnccnttcg	540
aattgcccgt	cncnngttn	ngaattgttc	cnaaaccacg	gttggtctcc	ccaggtcncc	600
tcttacggaa	gggcctgggc	cnctttncaa	ggttggggga	accnaaaatt	tcncttntgc	660
ccnccncca	cnntcttgng	nnncanttt	ggaacccttc	cnattccctt	tggectenna	720
ncctttncta	anaaaacttn	aaancgtngc	naaanmttn	acttcccccc	ttacc	775

&lt;210&gt; 26

&lt;211&gt; 820

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(820)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 26

anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanagata	ncttatnca	acagtgtctt	gaccaagagc	tgctgggcac	atttcttgca	120
gaaaagggtg	cggtcccat	cactcctcct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcggtggga	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcgggag	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
nctgaggggt	cacactataa	acgttaacga	ccnagatnan	cacctgtctc	aagtgcaccc	360
ttcctacctg	acnaccagng	accnnaact	gcngcctggg	gacagcnctg	ggancagcta	420
acnnagcact	cacctgcccc	cccatggccg	tnccgntccc	tggtcctgnc	aaggaagct	480

ccctgttgga	attncgggga	naccaaggga	nccccctcct	ccanctgtga	aggaaaaann	540
gatggaattt	tncccttccg	gccnntcccc	tcttccttta	cacgccccct	nntactctnc	600
tccctctntt	ntcctgncnc	acttttnacc	ccnnnatttc	ccttnattga	tcggannctn	660
ganattccac	tnnccgctnc	cntcnatcng	naanacnaaa	nactntctna	cccnggggat	720
gggnccctcg	ntcatcctct	ctttttcnct	acnccnntt	ctttgcctct	ccttngatca	780
tccaaccntc	gntggccntn	ccccccnnn	tcctttncce			820

&lt;210&gt; 27

&lt;211&gt; 818

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(818)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 27

tctgggtgat	ggcctcttcc	tcctcagggga	cctctgactg	ctctgggcca	aagaatctct	60
tgtttcttct	ccgagcccca	ggcagcgggtg	attcagccct	gcccacactg	attctgatga	120
ctgcggtatgc	tgtgacggac	ccaaggggca	aatagggtcc	caggggtccag	ggagggggcg	180
ctgctgagca	cttcggcccc	tcacctgcc	cagccccctgc	catgagctct	gggctgggtc	240
tcggcctcca	gggttctgct	cttccangca	ngccancaaag	tgccgctggg	ccacactggc	300
ttcttctgct	ccctccctgc	gctctganc	tctgtcttcc	tgctctgtgc	angcnccttg	360
gatctcagtt	tcctctcnct	anngaactct	gtttctgann	tcttcantta	actntgantt	420
tatnacnna	tggnctgtnc	tgctcnaactt	taatgggccc	gaccggctaa	tcctctccctc	480
ntcccttcc	anttcnnnna	accngcttnc	cntctctcc	ccntancccg	ccngggaanc	540
ctcctttgcc	ctnaccangg	gccnnnaccg	ccctnnctn	ggggggcang	gtnnctncnc	600
ctgntnnccc	cncctcncnt	tnccctctcc	cnnccnccgc	nngcannntc	ncngtcccn	660
tnnctcttcn	ngntcgnaa	ngntcncntn	tnnnnnngcn	ngntnntncn	tcctctcnc	720
cnnntgnang	tnnttnnnnc	ncngnncccc	nnnnnnnnnn	nggnntnnnn	tctncncngc	780
cccncccccc	ngnatgaag	cctcnnatct	ccggccnc			818

&lt;210&gt; 28

&lt;211&gt; 731

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(731)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 28

aggaagggcg	gagggatatt	gtangggatt	gagggatagg	agnataangg	gggaggtgtg	60
tcccaacatg	anggtgnngt	tctcttttga	angagggttg	ngtttttann	ccnggtgggt	120
gattnaacc	cattgtatgg	agnnaaagg	tttnagggat	ttttcggctc	ttatcagtat	180
ntanattcct	gtnaatcgga	aaatnatntt	tcnnccngaa	aatnttgctc	ccatccgnaa	240
attnctccc	ggtagtgc	nttngggggn	cngccangtt	tcccaggctg	ctanaatcgt	300
actaaagnnt	naagtgggan	tncaaatgaa	aacctnnac	agagnatccn	taccgactg	360
tnnnntncct	tcgcccctntg	actctgcnn	agcccaatac	ccnnngngnat	gtcncccngn	420
nnngcgcnc	tgaannnnnc	tcgnggctnn	gancatcang	gggtttcgca	tcaaaagcnn	480
cgtttencat	naaggcaact	tngcctcatc	caaccnctng	ccctcnncca	tttngccgtc	540
nggttncct	acgctnnntg	cncctnnntn	ganattttnc	ccgcttnggg	naancctcct	600
gnaatgggta	gggnccttntc	ttttnacnn	gnggtntact	aatcnnctnc	acgctnctt	660
tctcnacccc	cccccttttt	caatcccanc	ggcnaatggg	gtctccccnn	cgangggggg	720
nnccccann	c					731

<210> 29  
 <211> 822  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(822)  
 <223> n = A,T,C or G

<400> 29  
 actagtccag tgtgggtgaa ttccattgtg ttggggncnc ttctatgant antnttagat 60  
 cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt 120  
 atntntacnc tcatanncct cnnnacccac tccctcttaa cccntactgt gcctatngcn 180  
 tnnctantct ntggcgcctn cnanccaccn gtggggcncac cncnngnatt ctcnatctcc 240  
 tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaancn 300  
 tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc 360  
 tactctgact cccacngcct annnattagc ancntccccc nacnatntct caaccaaadc 420  
 ntcaacaacc tatctantctg ttcnccaacc nttncctcgc atccccnnac aacccccctc 480  
 ccaaataccc nccacctgac ncctaaccn caccatcccg gcaagccnan ggnccatttan 540  
 ccactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600  
 aatnctcctn naatttactn ncantnccat caancccaen tgaaacnnaa cccctgtttt 660  
 tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc ccccnctnc 720  
 ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaaggcna anannntccg 780  
 canatcctat cccttanttn ggggnccctt ncccnngggc cc 822

<210> 30  
 <211> 787  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(787)  
 <223> n = A,T,C or G

<400> 30  
 cggccgcctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg 60  
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120  
 gtctgcagga ttfgatgtct gaagtcgttg agtgtggctt ggagctcctc atctacatna 180  
 gctggaagcc ctggagggcc tctctcgcca gcctccccct tctctccacg ctctccangg 240  
 acaccagggg ctccaggcag cccattatct ccagnangac atgggtgtttc tccacgcgga 300  
 cccatggggc ctgnaaggcc aggtctcctt ttgacacccat ctctcccgtc ctgctgggca 360  
 ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt 420  
 tcccnttaat gaagggttaat tgcncgcttg gcgtaatcat nggtcanaac tntttcctgt 480  
 gtgaaattgt ttntcccctc ncnattccnc ncnacatacn aaccgggaan cataaagtgt 540  
 taaagcctgg ggtngcctn nngaanaaac tnaactcaat taattgcgtt ggctcatggc 600  
 ccgctttccn ttcnngaaaa ctgtcntccc ctgcnttntt gaatcgggca ccccccnggg 660  
 aaaagcggtt tgcnttttng ggggntcctt ccncttcccc cctcnctaan ccctncgect 720  
 cggtcgttnc nggtngcggg gaangggnat nnnctccnc naagggggng agnnngntat 780  
 ccccaaa 787

<210> 31  
 <211> 799  
 <212> DNA  
 <213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(799)  
 <223> n = A,T,C or G

<400> 31

tttttttttt	tttttttggc	gatgctactg	tttaattgca	ggagggtggg	gtgtgtgtac	60
catgtaccag	ggctattaga	agcaagaagg	aaggaggag	ggcagagcgc	cctgctgagc	120
aacaaaggac	tcctgcagcc	ttctctgtct	gtctcttggc	gcaggcacat	ggggaggcct	180
cccgcagggt	gggggccacc	agtccagggt	tgggagcact	acanggggtg	ggagtgggtg	240
gtggctggt	cnaatggcct	gncacanatc	cctacgattc	ttgacacctg	gatttcacca	300
ggggaccctc	tggtctccca	nggnaacttc	ntnnatctcn	aaagaacaca	actgtttctt	360
cngcanttct	ggctgttcac	ggaaagcaca	ggtgtccnat	ttnggctggg	acttgggtaca	420
tatggttccg	gcccacctct	cccntcnaan	aagtaattca	ccccccccc	ccntctnttg	480
cctgggccct	taantaccca	caccggaact	canttantta	ttbatcttng	gntgggcttg	540
ntnatcnccn	cctgaangcg	caaagttaga	aggccacgcc	gtncccnctc	cccatagnan	600
nttttncnt	cantctaatgc	ccccccnggc	aacnatccaa	tcccccccn	tgggggcccc	660
agccccangc	ccccgncctg	ggnnnccngn	cncgnantcc	ccagmntctc	ccantcngnc	720
ccnnngcncc	cccgcacgca	gaacanaagg	ntngagccnc	cgcannnnnn	nggtnncnac	780
ctcgcccccc	ccnnccgng					799

<210> 32  
 <211> 789  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(789)  
 <223> n = A,T,C or G

<400> 32

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
tttttncnag	ggcagggttta	ttgacaacct	cncgggacac	aancaggctg	gggacaggac	120
ggcaacaggc	tccggcgggc	gcggcgggcg	ccctacctgc	ggtaccaa	ntgcagcctc	180
cgctcccgt	tgatnttct	ctgcagctgc	aggatgccnt	aaaacagggc	ctcggccntn	240
ggtgggacc	ctgggatttn	aatttccacg	ggcacaatgc	ggtcgcancc	cctcaccacc	300
nattaggaat	agtggnttta	ccnccncccg	ttggcncact	ccccntggaa	accacttntc	360
gcggctccgg	catctggtct	taaaccttgc	aaacnctggg	gcctcttttt	tggttantnt	420
nccngccaca	atcatnactc	agactggcnc	gggctggccc	caaaaaancn	ccccaaaacc	480
ggnccatgtc	ttnnccgggt	tgctgcnatn	tncatcacct	ccccgggcna	ncaggncaac	540
ccaaaagtct	ttngggcccn	caaaaaanct	ccggggggnc	ccaagtttcaa	caaagtcac	600
ccccttgccc	cccaaatcct	ccccccgntt	nctgggtttg	ggaacccacg	cctctnnctt	660
tggnnggcaa	gntggntccc	ccttcggggc	cccgggtggc	ccnctcttaa	ngaaaacncc	720
ntcctnnnca	ccatcccccc	nngnnacgnc	tancaangna	tccctttttt	tanaaacggg	780
ccccccnccg						789

<210> 33  
 <211> 793  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(793)  
 <223> n = A,T,C or G

<400> 33

gacagaacat	ggtggatggt	ggagcacctt	tctatacgac	ttacaggaca	gcagatgggg	60
------------	------------	------------	------------	------------	------------	----

aattcatggc	tgttgagca	atanaacccc	agttctacga	gctgctgac	aaaggacttg	120
gactaaagtc	tgatgaactt	cccaatcaga	tgagcatgga	tgattggcca	gaaatgaana	180
agaagtttgc	agatgtat	gcaaagaaga	cgaaggcaga	gtggtgtcaa	atctttgacg	240
gcacagatgc	ctgtgtgact	ccggttctga	cttttgagga	ggttggtcat	catgatcaca	300
acaangaacg	gggctcggtt	atcaccantg	aggagcagga	cgtgagcccc	cgccctgcac	360
ctctgctgtt	aaacacccca	gccatccctt	ctttcaaaag	ggatccacta	cttctagagc	420
ggncgccacc	gcggtggagc	tccagctttt	gtcccttta	gtgaggggta	attgcgcgct	480
tggcgtaatc	atggtcatan	ctgtttcctg	tgtagaattg	ttatccgctc	acaattccac	540
acaacatacg	anccggaagc	atnaaat	aaagcctggn	ggtngcctaa	tgantgaact	600
naetacatt	aattggcttt	gcgctcactg	cccgtttcc	agtcgggaaa	acctgtcctt	660
gccagctgcc	nttaatgaat	cnggccaccc	cccggggaaa	aggcngtttg	cttnttgggg	720
cgcnettc	gctttctcgc	ttcctgaant	ccttccccc	ggtctttcgg	cttgccgcna	780
acggtatcna	cct					793

&lt;210&gt; 34

&lt;211&gt; 756

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(756)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 34

gccgcgaccg	gcatgtacga	gcaactcaag	ggcgagtggga	accgtaaaag	ccccaatctt	60
ancaagtgcg	gggaanagct	gggtcgactc	aagctagt	ttctggagct	caacttcttg	120
ccaaccacag	ggaccaagct	gaccaaacag	cagctaattc	tgcccggtga	catactggag	180
atcggggccc	aattggagcat	cctacgcaan	gacatccct	ccttcgagcg	ctacatggcc	240
cagctcaaat	gctactactt	tgattacaan	gagcagctcc	ccgagtcagc	ctatatgcac	300
cagctcttgg	gcctcaacct	cctcttctctg	ctgtcccaga	accgggtggc	tgantnccac	360
acgganttgg	ancggctgcc	tgcccaanga	catacanacc	aatgtctaca	tcnaccacca	420
gtgtcctgga	gcaatactga	tgganggcag	ctaccncaa	gtnttcctgg	ccnagggtaa	480
catccccgcg	cgagagctac	accttcttca	ttgacatcct	gctcgacact	atcaggggatg	540
aaaatcgng	ggttgctcca	gaaagctnc	aanaanatcc	ttttnctga	aggcccccg	600
atnncnctagt	nctagaatcg	gcccgccatc	gcggtgganc	ctccaacctt	tcgttnccct	660
ttactgaggg	ttnattgccg	cccttggcgt	tatcatggtc	acncngttn	cctgtgttga	720
aattnttaac	ccccacaa	tccacgcna	cattng			756

&lt;210&gt; 35

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(834)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 35

ggggatctct	anatcnacct	gnatgcatgg	ttgtcggtgt	ggtcgctgtc	gatgaanatg	60
aacaggatct	tgcccttgaa	gctctcggt	gctgtnttta	agttgctcag	tctgccgtca	120
tagtcagaca	cnctcttggg	caaaaaacan	caggatntga	gtcttgattt	cacctccaat	180
aatcttcngg	gctgtctgct	cggtgaactc	gatgacnang	ggcagctggg	tgtgntgat	240
aaantccanc	angttctcct	tggtgacctc	cccttcaaag	ttgttccggc	cttcatcaaa	300
cttctnnaan	angannancc	cantttgtc	gagctggnat	ttgganaaca	cgtcactgtt	360
ggaaactgat	cccaaagtgt	atgtcatcca	tcgcctctgc	tgcttgcaaa	aaacttgctt	420
ggcncaaate	cgactcccn	tccttgaaag	aagccnatca	cacccccctc	cctggactcc	480

nncaangaact	ctnccgctnc	cccntccnng	cagggttggt	ggcannccgg	gcccntgcgc	540
ttcttcagcc	agttcacnat	nttcacagc	ccctctgcc	gctgttntat	tccttggggg	600
ggaancogtc	tctcccttc	tgaannaact	ttgaccgtng	gaatagccgc	gcntcncnt	660
acntnctggg	ccgggttcaa	antccctccn	ttgncnntcn	cctcggggcca	ttctggattt	720
nccnaacttt	ttccttcccc	cnccccncgg	ngtttggnnt	tttcatnggg	ccccaaactct	780
gctnttggcc	antccctgg	gggcntntan	cnccccctnt	ggtcccntng	ggcc	834

&lt;210&gt; 36

&lt;211&gt; 814

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(814)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 36

cgngcgttt	ccngccgcgc	cccgtttcca	tgacnaaggc	tcctttcang	ttaaatacnn	60
cctagnaacc	attaatgggt	tgctctacta	atacatcata	cnaaccagta	agcctgcccc	120
naacgccaac	tcaggccatt	cctaccaaag	gaagaaaggc	tggtctctcc	acccctgtga	180
ggaaaggcct	gccttgtaag	acaccacaat	ncggctgaat	ctnaagtctt	gtgttttact	240
aatggaaaaa	aaaaataaac	aanaggtttt	gttctcatgg	ctgcccaccg	cagcctggca	300
ctaaaacanc	ccagcgctca	cttctgcttg	ganaaatatt	ctttgctctt	ttggacatca	360
ggcttgatgg	tatcaactgc	acntttccac	ccagctgggc	ncccttcccc	catntttgtc	420
antganctgg	aaggcctgaa	ncttagtctc	caaaagtctc	ngcccacaag	accggccacc	480
aggggagctc	ntttncagtg	gatctgccaa	anantaccn	tatcatcnnt	gaataaaaag	540
gcccctgaac	ganatgcttc	cancancctt	taagaccat	aatcctngaa	ccatggtgcc	600
cttccggtct	gatecnaaag	gaatgttctt	gggtcccant	ccctcctttg	ttnccttacgt	660
tgtnttggac	ccntgctngn	atnacccaan	tganatcccc	ngaagcacc	tnccctggc	720
atttganttt	cntaaattct	ctgcctacn	nctgaaagca	cnattccctn	ggcncnaan	780
ggngaactca	agaaggtctn	ngaaaaacca	cncn			814

&lt;210&gt; 37

&lt;211&gt; 760

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(760)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 37

gcatgctgct	cttctcctcaa	gttgttcttg	ttgccataac	aaccaccata	ggtaaagcgg	60
gcgcagtggt	cgctgaagg	gttgtagtag	cagcgcgga	tgctctcctt	gcagagtcct	120
gtgtctggca	ggtccacgca	atgccctttg	tcactgggga	aatggatgcg	ctggagctcg	180
tcnaanccac	tcgtgtattt	ttcacangca	gcctcctccg	aagntccgg	gcagttgggg	240
gtgtcgtcac	actccactaa	actgtcgatn	cancagccca	ttgctgcagc	ggaactgggt	300
gggctgacag	gtgccagaac	acactggatn	ggcctttcca	tgaagggcc	tgggggaaat	360
cncctnanc	caaactgcct	ctcaaggcc	accttgaca	ccccgacagg	ctagaaatgc	420
actcttcttc	ccaaggtag	ttgttcttgt	tgcccaagca	nctccanca	aaccaaaanc	480
ttgcaaaatc	tgctccgtgg	gggtcatnnn	taccanggtt	ggggaaanaa	acccggcngn	540
ganccnccct	gtttgaatgc	naaggnaata	atcctctgt	cttgcttggg	tggaaanagca	600
caattgaact	gttaacnttg	ggccngttc	cncnngggtg	gtctgaaact	aatcaccgtc	660
actggaaaaa	ggtangtgc	ttccttgaat	tcccaaannt	cccctngntt	tgggtntttt	720
ctcctctncc	ctaaaaatcg	tnttcccccc	ccntanggcg			760



<210> 38  
 <211> 724  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(724)  
 <223> n = A,T,C or G

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<400> 38
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cttcnnaaat tgtccaaccc cctcnnccaa atnnccattt cggggggggg gttccaaacc    120
caaattaatt ttgganttta aattaaatnt tnatnggggg aanaanccaa atgtnaagaa    180
aatttaaccc attatnaact taaatncctn gaaacccntg gnttccaaaa atttttaacc    240
cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt    300
ngatttaaac ccccttnant tnttttnacc cnnngctnaa ntatttngnt tccggtgttt    360
tcctnttaan cntnggtaac tcccgntaat gaannncctt aanccaatta aaccgaattt    420
tttttgaatt ggaaattccn ngggaattna cgggggtttt tcccnttttg gggccatncc    480
ccncttttgg ggtgttgggn ntaggttgaa tttttnnang nccccaaaaa ncccccaana    540
aaaaaactcc caagnnttaa ttngaattnc ccccttccca ggccttttgg gaaaggnggg    600
ttnttggggg ccngggantt cnttccccc ttnccncccc cccccnggt aaanggttat    660
ngnntttggt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccgggncg    720
gccg                                           724
  
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<210> 39  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

```

<400> 39
tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca    60
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt    120
tttattttatt tttactgaaa gtgagaggga acttttgggg ccttttttcc tttttctgta    180
ggcgcgctta agcttttctaa atttggaaac tctaagcaag ctgaanggaa aaggggggtt    240
cgcaaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga    300
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttttaattana    360
cttgggggtt ccttccccc accaaccncc ctgacaaaaa gtgcngccc tcaaatnatg    420
tcccggnnt cnttgaaaca cacngcngaa ngttctcatt ntccccncnc caggtnaaaa    480
tgaagggtta ccatntttta cncacctcc acntggcnnn gcctgaatcc tcnaaaancn    540
ccctcaancn aattnctnng ccccggtcnc gcntnngtcc cnccggggt ccgggaantn    600
cacccccnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc    660
cnnagactnt cctcnncnan cncaattttc tttntntcac gaacncgnnc cnnaaaatgn    720
nnnnncctc cncngtccn naatcnccan c                                           751
  
```

<210> 40  
 <211> 753  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(753)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 40

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agatgaaa	acccccg	agacagc	actgcca	agcagccg	gtaggagg	ggg	120
cgccctat	gcacagct	gggc ccttgag	acagggc	ttc gatgtc	aggc tcatgt	caa	180
tggctcgg	aa gggcggt	cgtacgt	acgggca	ccagggc	accaggaa	act	240
tctcaaagt	ccaggca	acn tgggtgc	acacggg	agacccag	gtatn agctt	gggg	300
cggtcata	aan cgcggtg	ggc tgcgt	ggagctg	ggcgc aggaag	gcna		360
ataaaagg	tg cgcggcg	ca ccgttc	anct cgcactt	ctc naanacc	atg angtt	gggt	420
cnaacccc	cacc accann	cgg acttcct	tga nggaatt	ccc aaatctc	ttc gntctt	gggc	480
ttctnctg	at gccctan	ctg gttgcc	cngn atgcca	ancca nccc	caancc	cggtgc	540
aaanaccc	cn cctctcn	tt tcatct	gggt tntntc	cccc ggacnt	gggt tctctc	aaag	600
gganccca	tata tctnacc	an tactcac	cnt ncccc	ccnt gnnacc	canc cttctan	ngn	660
ttccnccc	cg ncctctg	ggc cntcaa	anan gcttnca	cna cctgggt	ctg ccttcccc		720
tnccctat	ct gnaccc	cn tttgtct	can tnt				753

&lt;210&gt; 41

&lt;211&gt; 341

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 41

actatat	cca tcaca	acaga catg	cttcat cccat	agact tcttg	acata gcttcaa	atg	60
agtgaa	ccca tcctt	gatatt atata	catat atgtt	ctcag tatttt	ggga gccttt	ccac	120
ttcttta	aac cttgt	tcat atga	aaactg aaaa	taggaa tttgt	gaaga gttaaa	aagt	180
tatagct	tgt ttacg	tagta agttt	ttgaa gtctac	attc aatcc	agaca cttagt	tgag	240
tgttaaa	ctg tgatt	tttaa aaa	atatcat ttgag	aatat tcttt	cagag gtattt	cat	300
ttttact	tttt tgatt	aattg tgttt	tatat attag	ggtag t			341

&lt;210&gt; 42

&lt;211&gt; 101

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 42

acttact	gaa tttagt	ctctg tgctct	tcct tatttag	tgtat	cataa atacttt	gat	60
gtttcaa	aca ttctaa	ataa ataatt	tttca gtggtt	cat a			101

&lt;210&gt; 43

&lt;211&gt; 305

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 43

acatcttt	gt tacagt	tctaa gatgt	gttct taaat	cacca ttcctt	cctg gtcc	caccc	60
tccagggt	tg tctcac	actg taatt	agagc tattg	aggag tcttt	acagc aaatta	aagt	120
tcagatgc	cct tgcta	agct agag	ttctag agttat	gttt cagaaa	gtct aagaa	accca	180
cctcttg	aga ggtcag	taaa gaggac	ttaa tatttc	atat ctacaaa	atg accac	aggat	240
tggtacag	a acgag	agtta tcttg	ataa ctcag	agct agtac	cctgcc	cgggg	300
tcgaa							305

&lt;210&gt; 44

&lt;211&gt; 852

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

<221> misc\_feature  
 <222> (1)...(852)  
 <223> n = A,T,C or G

<400> 44

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gattatttgg	tgtgtgtttt	ggtttgtgtc	caaagtattg	gcagcttcag	ttttcatttt	120
ctctccatcc	tggggcattc	ttcccaaatt	tatataccag	tcttcgtcca	tccacacgct	180
ccagaatttc	tctttttag	taatattctca	tagctcggct	gagcttttca	taggtcatgc	240
tgtgttgttt	cttcttttta	ccccatagct	gagccactgc	ctctgatttc	aagaacctga	300
agacgccctc	agatcggctc	tcccatttta	ttaatcctgg	gttcttgtct	gggttcaaga	360
ggatgtcgcg	gatgaattcc	cataagttag	tccctctcgg	gttgtgcttt	ttggtgtggc	420
acttggcagg	gggtgtttgc	tcttttttca	tatcagggtga	ctctgcaaca	ggaaggtgac	480
tgtgtgttgt	catggagatc	tgagcccggc	agaaagtttt	gctgtccaac	aaatctactg	540
tgctaccata	gttgtgtgtca	tataaatagt	tctngtcttt	ccagggtgtc	atgatggaag	600
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actggccggt	ccacttcaga	tgctgcaagt	tgctgtagag	gagntgcccc	gccgtccctg	720
ccgccgggt	gaactcctgc	aaactcatgc	tgcaaagggt	ctcgccgttg	atgtcgaact	780
cntggaaagg	gatacaattg	gcattccagct	ggttgggtgc	caggaggtga	tggagccact	840
cccacacctg	gt					852

<210> 45  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

<400> 45

acaacagacc	cttgctcgct	aacgacctca	tgctcatcaa	gttggacgaa	tccgtgtccg	60
agtctgacac	catccggagc	atcagcattg	cttcgcagtg	ccctaccgcg	gggaactctt	120
gcctcgtttc	tggctggggg	ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	180
tgaacgtgtc	ggtgtgtgtc	gaggaggtct	gcagtaagct	ctatgacccg	ctgt	234

<210> 46  
 <211> 590  
 <212> DNA  
 <213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(590)  
 <223> n = A,T,C or G

<400> 46

actttttatt	taaatgttta	taaggcagat	ctatgagaat	gatagaaaac	atggtgtgta	60
atttgatagc	aatatttttg	agattacaga	gttttagtaa	ttaccaatta	cacagttaaa	120
aagaagataa	tatattccaa	gcanatacaa	aatatctaat	gaaagatcaa	ggcaggaaaa	180
tgantataac	taattgacaa	tggaaaatca	attttaatgt	gaattgcaca	ttatccttta	240
aaagctttca	aaanaanaaa	ttattgcagt	ctanttaatt	caaacagtgt	taaatgggtat	300
caggataaan	aactgaaggg	canaaagaat	taattttcac	ttcatgtaac	ncacccanat	360
ttacaatggc	ttaaatgcan	ggaaaaagca	gtggaagtag	ggaagtantc	aaggctcttc	420
tggctctctaa	tctgccttac	tctttgggtg	tggctttgat	cctctggaga	cagctgccag	480
ggctcctgtt	atatccacaa	tcccagcagc	aagatgaagg	gatgaaaaag	gacacatgct	540
gccttccttt	gaggagactt	catctcactg	gccaacactc	agtcacatgt		590

<210> 47  
 <211> 774  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(774)  
 <223> n = A,T,C or G

<400> 47  
 acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60  
 tgaacagaat tttcctgnac aacgggggctt caaaataatt ttcttgggga gggtcaagac 120  
 gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180  
 cattacagac gggactctgg gaggaaggat aaacagaaaag gggacaaaag ctaatcccaa 240  
 aacatcaaag aaaggaagggt ggcgtcatat ctcccagcct acacagttct ccagggtctt 300  
 cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtg 360  
 ctggctctg gtcttcagcc cccagctctg gaagcccacc ctctgtgat cctgcgtggc 420  
 ccacactcct tgaacacaca tccccagggt atattcctgg acatggctga acctcctatt 480  
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540  
 acggcatggg aagcctttct gacttgcctg attactccag catcttgga caatccctga 600  
 ttccccactc cttagaggca agatagggtg gttaagagta gggctggacc acttgagcc 660  
 aggctgctgg cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct 720  
 tcaattctat gggcntcatt ttgttctacc tgcaaatgg gggataataa tagt 774

<210> 48  
 <211> 124  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(124)  
 <223> n = A,T,C or G

<400> 48  
 canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60  
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120  
 tgggt 124

<210> 49  
 <211> 147  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(147)  
 <223> n = A,T,C or G

<400> 49  
 gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt 60  
 tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120  
 ttagggcacc catatcccaa gcantgt 147

<210> 50  
 <211> 107  
 <212> DNA  
 <213> Homo sapien

<400> 50  
 acattaaatt aataaaagga ctgttgggggt tctgctaaaa cacatggctt gatatttgc 60

atggtttgag gttaggagga gttaggcata tgttttggga gaggggt

107

<210> 51  
 <211> 204  
 <212> DNA  
 <213> Homo sapien

<400> 51  
 gtcctaggaa gtctagggga cacacgactc tgggggtcacg gggccgacac acttgacagg 60  
 cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120  
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgcc cacttgcca 180  
 ctcctctttt gggaccagca atgt 204

<210> 52  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(491)  
 <223> n = A,T,C or G

<400> 52  
 acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaagggtta gtattgtgta 60  
 gggatatttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120  
 ccatcagaca ggtttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180  
 aaaacttctt gtatcaattt cttttgttca aaatgactga ctttaantatt tttaaatatt 240  
 tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtnc ctcagtccca 300  
 atgttgctca gataaataa tctcgtgaga acttaccacc caccacaagc tttctggggc 360  
 atgcaacagt gtcttttctt tnccttttct tttttttttt ttacaggcac agaaactcat 420  
 caattttatt tggataacaa aggggtctcca aatttatattg aaaaaataat ccaagttaat 480  
 atcactcttg t 491

<210> 53  
 <211> 484  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(484)  
 <223> n = A,T,C or G

<400> 53  
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60  
 gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac 120  
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180  
 caatcaaatc tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct 240  
 gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300  
 agctttgant ttccttgtgc tgatangagg aaaggctgaa ttaccttggt gcctctccct 360  
 aatgattgyc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg 420  
 tanccttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc 480  
 cant 484

<210> 54  
 <211> 151  
 <212> DNA

<213> Homo sapien

<400> 54

actaaacctc gtgcttgga actccatata gaaaacgggtg ccatccctga acacggctgg	60
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag	120
tctatgtcct ctcaagtgcc tttttgtttg t	151

<210> 55

<211> 91

<212> DNA

<213> Homo sapien

<400> 55

acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc	60
gccctccagt ggatactga gccaaagtgg t	91

<210> 56

<211> 133

<212> DNA

<213> Homo sapien

<400> 56

ggcggatgtg cggttggtat atacaaatat gtcattttat gtaagggact tgagtatact	60
tggttttttg gtatctgtgg gttgggggga cggtcagga accaataccc catggatacc	120
aagggacaac tgt	133

<210> 57

<211> 147

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(147)

<223> n = A,T,C or G

<400> 57

actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc	60
gactgggagc tgagcccttc cttttgcgcc tgccctcagag gattgttgcc gacntgcana	120
tctcantggg ctggatncat gcagggt	147

<210> 58

<211> 198

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(198)

<223> n = A,T,C or G

<400> 58

acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc	60
tgattacata catttatcct ttaaaaaaga tgtaaatctt aatttttatg ccatctatta	120
atttaccat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt	180
ttgacttcta agtttgggt	198

<210> 59

<211> 330  
 <212> DNA  
 <213> Homo sapien

<400> 59  
 acaacaaatg gggtgtgagg aagtcttatac agcaaaactg gtgatggcta ctgaaaagat 60  
 ccattgaaaa ttatcattaa tgatttttaa tgacaagtta tcaaaaactc actcaatttt 120  
 cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180  
 tacagtcaat aaatgacaaa gccagggcct acaggtgggt tccagacttt ccagaccag 240  
 cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt 300  
 tttcgtcttt attggacttc tttgaagagt 330

<210> 60  
 <211> 175  
 <212> DNA  
 <213> Homo sapien

<400> 60  
 accgtgggtg ccttctacat tcctgacggc tccttcacca acatctgggt ctacttcggc 60  
 gtcgtgggct ccttcctctt catcctcatc cagctgggtg tgctcatcga ctttgcgcac 120  
 tcctggaacc agcgggtggc gggcaaggcc gaggagtgcg attcccggtc ctggt 175

<210> 61  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 61  
 accccaactt tcctcctgtg agcagtctgg acttctcact gctacatgat gaggggtgagt 60  
 ggttggtgct cttcaacagt atcctccctt ttccggatct gctgagccgg acagcagtgc 120  
 tggactgcac agccccgggg ctccacattg ctgt 154

<210> 62  
 <211> 30  
 <212> DNA  
 <213> Homo sapien

<400> 62  
 cgctcgagcc ctatagtga tcgtattaga 30

<210> 63  
 <211> 89  
 <212> DNA  
 <213> Homo sapien

<400> 63  
 acaagtcatt tcagcacctt ttgtcttcca aaactgacca tcttttatat ttaatgcttc 60  
 ctgtatgaat aaaaatggtt atgtcaagt 89

<210> 64  
 <211> 97  
 <212> DNA  
 <213> Homo sapien

<400> 64  
 accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag 60  
 aatcagtgc tccaggattg gtccctggat ctgggggt 97

25

<210> 65  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(377)  
 <223> n = A,T,C or G

<400> 65  
 acaacaanaa ntcccttctt taggccaactg atggaaacct ggaacccct tttgatggca 60  
 gcatggcgctc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc 120  
 ccaaccctgg tctaccaca nttctggcta tgggctgtct ctgccactga acatcagggt 180  
 tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa 240  
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg 300  
 tgggggtgaa ctacccccc gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360  
 gggcgggagg agcatgt 377

<210> 66  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 66  
 acgcctttcc ctccagaattc agggaagaga ctgtgcctg ccttcctcgg ttgttgctg 60  
 agaaccctgt tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120  
 aggaactaac tgcaccctgg tccctcctccc agtccccagt tcaccctcca tccctcacct 180  
 tccctcactc taaggatata caacactgcc cagcacaggg gccctgaatt tatgtgggtt 240  
 ttatatattt ttttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
 tgttt 305

<210> 67  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<400> 67  
 actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120  
 ccccttttaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
 tgtgtgtgtc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240  
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgccatac 360  
 catagtttct gtgctagtgg accgt 385

<210> 68  
 <211> 73  
 <212> DNA  
 <213> Homo sapien

<400> 68  
 acttaaccag atatatattt accccagatg gggatattct ttgtaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA



<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttgggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccgggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcggtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagagggtgg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaac	480
gaangtcct	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgacccta	acaggggcc	tctcagccct	cctaataacc	tccggcctag	ccatgtgatt	60
tcacttcac	tccataacgc	tcctcactac	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatagc	ggataatcct	atttattacc	tcagaagtgt	ttttcttcgc	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	tcccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atccccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcacagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttca	taacttaaaa	agtgaatttg	aaaaagaaaa	tctccagcaa	gcattctcatt	240
taaataaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tatttttaaa	aagtacatgg	480
taaaaaaaaa	aattcacaac	agtatataag	gctgtaaaaa	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(511)  
 <223> n = A,T,C or G

<400> 72

tattacggaa	aaacacacca	cataattcaa	ctancaaaga	anactgcttc	agggcgtgta	60
aaatgaaaag	cttccaggca	gttatctgat	taaagaacac	taaaagagg	acaaggctaa	120
aagccgcagg	atgtctacac	tatancaggc	gctatttggg	ttggctggag	gagctgtgga	180
aaacatggan	agattggtgc	tgganacgc	cgtggctatt	cctcattggt	attacanagt	240
gaggttctct	gtgtgcccac	tggtttgaaa	accgttctnc	aataatgata	gaatagtaca	300
cacatgagaa	ctgaaatggc	ccaaaccag	aaagaaagcc	caactagatc	ctcagaanac	360
gcttctaggg	acaataaccg	atgaagaaaa	gatggcctcc	ttgtgcccc	gtctgttatg	420
atttctctcc	attgcagcna	naaacccgtt	cttctaagca	aacncagggtg	atgatggcna	480
aaatacacc	cctcttgaag	naccnggagg	a			511

<210> 73  
 <211> 499  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(499)  
 <223> n = A,T,C or G

<400> 73

cagtgcagc	actggtgcc	gtaccagtac	caataacagt	gccagtgcc	gtgccagcac	60
cagtgggtgc	ttcagtgtg	gtgccagcct	gaccgccact	ctcacatttg	ggctcttcgc	120
tggccttgg	ggagctggg	ccagcaccag	tggcagctct	ggtgcctgtg	gtttctccta	180
caagtgaag	tttagatatt	gttaatcctg	ccagtctttc	tcttcaagcc	aggggtgcatc	240
ctcagaaacc	tactcaacac	agcactctag	gcagccacta	tcaatcaatt	gaagttgaca	300
ctctgcatta	aatctatttg	ccatttctga	aaaaaaaaaa	aaaaaaagg	cggccgctcg	360
antctagagg	gcccgtttaa	accgctgat	cagcctcgac	tgtgccttct	anttgccagc	420
catctgttgt	ttgccctcc	cccgtgcct	tccttgaccc	tggaaagtgc	cactccact	480
gtcctttcct	aantaaaat					499

<210> 74  
 <211> 537  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(537)  
 <223> n = A,T,C or G

<400> 74

tttcatagga	gaacacactg	aggagatact	tgaagaattt	ggattcagcc	gcgaagagat	60
ttatcagctt	aactcagata	aaatcattga	aagtaataag	gtaaaagcta	gtctctaact	120
tccaggccca	cggctcaagt	gaatttgaat	actgcattta	cagtgtagag	taacacataa	180
cattgtatgc	atggaacat	ggaggaacag	tattacagt	tcctaccact	ctaatacaaga	240
aaagaattac	agactctgat	tctacagtga	tgattgaatt	ctaaaaatgg	taatcattag	300
ggcttttgat	ttataanact	ttgggtactt	atactaaatt	atggtagtta	tactgccttc	360
cagtttgctt	gatatatttg	ttgatattaa	gattcttgac	ttatatattg	aatgggttct	420
actgaaaaan	gaatgatata	ttcttgaaga	catcgatata	catttattta	cactcttgat	480
tctacaatgt	agaaaatgaa	ggaaatgcc	caaattgtat	ggtgataaaa	gtcccg	537

<210> 75  
 <211> 467  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60  
 tgcataattac acgtacctcc tcctgctcct caagtagtgt ggtctatttt gccatcatca 120  
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagcgt cttctgagga 240  
 tctagtggg ctttctttct gggtttgggc catttcantt ctcattgtgt tactattcta 300  
 tcattattgt ataacggtt tcaaacngt gggcacncag agaacctcac tctgtaataa 360  
 caatgaggaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc 420  
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
 aagctgacag cattcgggcc gagatgtctc gtcctgtggc cttagctgtg ctgcgctac 60  
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcaggtt tactcacgtc 120  
 atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag 240  
 acttgtcttt cagcaaggac tggcttttct atctcttcta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
 ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgtgc 120  
 caggcaactgt tcatctcagc ttttctgtcc ctttgctccc ggcaagcgtc tctgctgaaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggtcc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78

actagtccag	tgtggtggaa	ttccattgtg	ttgggcccaa	cacaatggct	acctttaaca	60
tcaccagac	ccgcccctgc	cgtgcccga	cgctgctgct	aacgacagta	tgatgcttac	120
tctgtactc	ggaaactatt	tttatgtaat	taatgtatgc	tttcttggtt	ataaatgcct	180
gatttaaaaa aaaaaaaaaa a						201

&lt;210&gt; 79

&lt;211&gt; 552

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(552)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 79

tccttttgtt	aggtttttga	gacaacccta	gacctaaact	gtgtcacaga	cttctgaatg	60
tttaggcagt	gctagtaatt	tcctcgtaat	gattctgtta	ttactttcct	attctttatt	120
cctctttctt	ctgaagatta	atgaagttga	aaattgaggt	ggataaatat	aaaaaggtag	180
tgtgatagta	taagtatcta	agtgcagatg	aaagtgtgtt	atatatatcc	attcaaaaatt	240
atgcaagtta	gtaattactc	agggttaact	aaattacttt	aatatgctgt	tgaacctact	300
ctgttccttg	gctagaaaaa	attataaaca	ggactttgtt	agtttgggaa	gccaaattga	360
taatattcta	tggttctaaa	gttgggctat	acataaanta	tnaagaaata	tggaatttta	420
ttccaggaa	tatggggttc	atttatgaat	antaccggg	anagaagttt	tgantnaaac	480
cngttttggt	taatacgta	atatgtcctn	aatnaacaag	gcntgactta	tttccaaaaa	540
aaaaaaaaaa aa						552

&lt;210&gt; 80

&lt;211&gt; 476

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(476)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 80

acagggattt	gagatgctaa	ggccccagag	atcgtttgat	ccaaccctct	tattttcaga	60
ggggaaaatg	gggcctagaa	gttacagagc	atctagctgg	tgcgctggca	cccctggcct	120
cacacagact	cccagtagtc	tgggactaca	ggcacacagt	cactgaagca	ggccctgttt	180
gcaattcacg	ttgccacctc	caacttaaac	attcttcata	tgtgatgtcc	ttagtcacta	240
aggttaaact	ttcccaccca	gaaaaggcaa	cttagataaa	atcttagagt	actttcatac	300
tcttctaagt	cctcttccag	cctcactttg	agtctctcct	gggggttgat	aggaantntc	360
tcttggcttt	ctcaataaaa	tctctatcca	tctcatgttt	aatttggtag	gcntaaaaat	420
gctgaaaaaa	ttaaaatggt	ctggtttcnc	tttaaaaaaa	aaaaaaaaaa	aaaaaa	476

&lt;210&gt; 81

&lt;211&gt; 232

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(232)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 81

```

tttttttttg tatgcentcn ctgtggngtt attgttgctg ccaccctgga ggagcccagt    60
ttctttctgta tctttctttt ctgggggatc ttcttggtc tgccctcca ttccagcct    120
ctcatcccca tcttgcaact ttgctagggt tggaggcgt ttcttgtag cccctcagag    180
actcagtcag cgggaataag tcttaggggt ggggggtgtg gcaagccggc ct          232

```

&lt;210&gt; 82

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 82

```

aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc    60
agtaccagta ccaataacat gccagtgccca gtgccagcac cagtgggtggc ttcagtgtc    120
gtgccagcct gaccgcact ctcacatttg ggctcttcgc tggccttggt ggagctggtg    180
ccagcaccag tggcagctct ggtgcctgtg gttctctcta caagtgagat tttagatatt    240
gttaatcttg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac    300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg    360
ccatttcaaa aaaaaaaaaa aaa          383

```

&lt;210&gt; 83

&lt;211&gt; 494

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(494)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 83

```

accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca    60
gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc    120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa    180
acgcttcaag gtgctcatga cccagcaacc gcgccctgtc ctctgagggt ccttaaactg    240
atgtcttttc tgccacctgt taccctcogg agactccgta accaaactct tcggactgtg    300
agccctgatg cctttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat    360
tatgcttgtg tgaggcaatc atggtggcat caccatnaa gggaaacacat ttgantttt    420
tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta    480
aaaaaaaaaa aaaa          494

```

&lt;210&gt; 84

&lt;211&gt; 380

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(380)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 84

```

gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca    60
agtatcctgc gcccgctctt ctaccgtccc tacctgcaga tcttcgggca gattccccag    120

```

```

gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgcaa ctggctgggtg 240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg 300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
agcgttnccg cctcatccgg 380

```

```

<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

```

```

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
tnccatcgct atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca 120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
tgtgaaagga tctccagaag gagtgtctga tcttcccac acttttgatg actttattga 240
gtcgattctg catgtccagc aggagggtgt accagctctc tgacagtgag gtcaccagcc 300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420
aaagaacacc tcctggaagt gctngccgct cctcgctcct tggtggnngc gcntnccttt 480
t 481

```

```

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 86
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
acttgaaaaa gcaacttnaa gcctggacac tggattataa attcacaata tgcaacactt 120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
atatntgagc ggaagantag cctttctact tcaccagaca caactccttt catattggga 420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

```

```

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

```

```

<400> 87

```

```

agaaccagt atctctnaaa acaacctctc ataccttggt gacctaatgt tgtgtgcgtg      60
tgtgtgtgcg cgcattat atagacaggc acatcttttt tacttttgta aaagcttatg      120
cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg      300
ggggacaaaag aaaaacanaa ctgaacatna gaaacaattn cctgggtgaga aattncataa      360
acagaaattg ggtngtatat tgaaananng catcattnaa acgttttttt ttt          413

```

&lt;210&gt; 88

&lt;211&gt; 448

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(448)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 88

```

cgcagcgggt cctctctatc tagctccagc ctctcgctg ccccaactcc cgcgtcccgc      60
gtcctagccn accatggcgc ggcccctgcg cgcgccgctg ctctgtctgg ccacccctggc      120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtcgc gcgaagccgc cgcgcctgggt      180
gggaggccca tggaccccgc gtggaagaag aagggtgtgc gcgtgcaact gactttgccg      240
tcggcnanta caacaaaccc gcaacnactt ttacnagcn cgcgtgcag gttgtgccgc      300
cccaancaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng      360
ttaccagaa ccnagccaat tngaacaatt ncccccat aacagcccct tttaaaaggg      420
gaancantcc tgncttttc caaat      448

```

&lt;210&gt; 89

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(463)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 89

```

gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca      60
gtagtgatcc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc      120
agagggtctag gtctgcatac cagcagacag ttgtccgtg tattttgtag ccttgaagtt      180
ctcagtgaca agttnnttct gatgcgaagt tctnattoca gtgttttagt cctttgcatc      240
tttnatgtn agacttgccct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg      300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaatn      360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn      420
aattcnnana anttcagtn tcatacaaca naacngganc ccc          463

```

&lt;210&gt; 90

&lt;211&gt; 400

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(400)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 90

agggattgaa	ggtctntnt	actgtcggac	tggtcancca	ccaactctac	aagttgctgt	60
cttccactca	ctgtctgtaa	gcntnttaac	ccagactgta	tcttcataaa	tagaacaaat	120
tcttcaccag	tcacatcttc	taggaccttt	ttggattcag	ttagtataag	ctcttccact	180
tcctttgtta	agacttcac	tggtaaagtc	ttaagttttg	tagaaaggaa	tttaattgct	240
cgttctctaa	caatgtcctc	tccttgaagt	atttggtgta	acaaccacc	tnaagtcct	300
ttgtgcatoc	attttaaata	tacttaatag	ggcattggtn	cactagggta	aattctgcaa	360
gagtcactctg	tctgcaaaaag	ttgcgttagt	atatctgccca			400

&lt;210&gt; 91

&lt;211&gt; 480

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(480)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 91

gagctcggat	ccaataatct	ttgtctgagg	gcagcacaca	tatncagtgc	catggnaact	60
ggtctacccc	acatgggagc	agcatgccgt	agntatataa	ggtcattccc	tgagtcagac	120
atgcctcttt	gactaccgtg	tgccagtgtt	ggtgattctc	acacacctcc	nnccgctctt	180
tggtgaaaaa	ctggcacttg	nctggaacta	gcaagacatc	acttaciaat	tcacccacga	240
gacacttgaa	aggtgtaaca	aagcgactct	tgcatgtctt	tttgtccctc	cggcaccagt	300
tgtcaatact	aaccgctggg	tttgctccca	tcacatttgt	gatctgtagc	tctggataca	360
tctcctgaca	gtactgaaga	acttcttctt	ttgtttcaaa	agcaactctt	ggtgcctgtt	420
ngatcaggtt	cccatttccc	agtcggaatg	ttcacatggc	atatnttact	tcccacaaaa	480

&lt;210&gt; 92

&lt;211&gt; 477

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(477)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 92

atacagccca	natccacca	cgaagatgcg	cttggtgact	gagaacctga	tgcggtcact	60
ggtcccgtctg	tagccccagc	gactctccac	ctgctggaag	cggttgatgc	tgcaactcctt	120
cccacgcagg	cagcagcggg	gccggtcaat	gaactccact	cgtggccttg	ggttgacggg	180
taantgcagg	aagaggctga	ccacctcgcg	gtccaccagg	atgcccgact	gtgcgggacc	240
tgacgcgaaa	ctcctcgatg	gtcatgagcg	ggaagcgaat	gangcccagg	gccttgccca	300
gaaccttccg	cctgttctct	ggcgtcacct	gcagctgctg	ccgctnacac	tcggcctcgg	360
accagcggac	aaacggcggt	gaacagccgc	acctcacgga	tgcccantgt	gtcgcgctcc	420
aggaacggcn	ccagcgtgtc	caggtcaatg	tcggtgaanc	ctccgcgggt	aatggcg	477

&lt;210&gt; 93

&lt;211&gt; 377

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(377)

&lt;223&gt; n = A,T,C or G



&lt;400&gt; 93

gaacggctgg	accttgccctc	gcattgtgct	gctggcagga	ataccttggc	aagcagctcc	60
agtccgagca	gccccagacc	gctgccgccc	gaagctaagc	ctgcctctgg	ccttccccctc	120
cgctcaatg	cagaaccant	agtgggagca	ctgtgttttag	agttaagagt	gaacactgtn	180
tgattttact	tgggaatttc	ctctgttata	tagcttttcc	caatgcta	ttccaaacaa	240
caacaacaaa	ataacatggt	tgccctgttna	gttgtataaa	agtangtgat	tctgtatnta	300
aagaaaatat	tactgttaca	tatactgctt	gcaanttctg	tattttattg	tnctctggaa	360
ataaatatat	tattaaa					377

&lt;210&gt; 94

&lt;211&gt; 495

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(495)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 94

ccctttgagg	ggttagggtc	cagttcccag	tggaagaaac	aggccaggag	aantgcgtgc	60
cgagctgang	cagatttccc	acagtgaccc	cagagccctg	ggctatagtc	tctgaccctc	120
ccaaggaaaag	accaccttct	ggggacatgg	gctggagggc	aggacctaga	ggcaccaagg	180
gaaggcccca	ttccggggct	gttccccgag	gaggaaggga	aggggctctg	tgtgcccccc	240
acgaggaana	ggccctgant	cctgggatca	nacacccctt	cacgtgtatc	cccacacaaa	300
tgcaagctca	ccaaggtccc	ctctcagtc	cttccctaca	ccctgaacgg	ncactggccc	360
acacccaccc	agancancca	cccgccatgg	ggaatgtntc	caaggaatcg	cngggcaacg	420
tggactctng	tcccnnaagg	gggcagaatc	tccaatagan	gganngaacc	cttgctnana	480
aaaaaaaaana	aaaaa					495

&lt;210&gt; 95

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(472)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 95

ggttacttgg	tttcattgcc	accacttagt	ggatgtcatt	tagaaccatt	ttgtctgctc	60
cctctggaag	ccttgcgag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	120
tagctgtttt	gagttgattc	gcaccactgc	accacaactc	aatatgaaaa	ctatttnact	180
tattttattat	cttgtgaaaa	gtatacaatg	aaaattttgt	tcatactgta	tttatcaagt	240
atgatgaaaa	gcaatagata	tatatctttt	tattatgttn	aattatgatt	gccattatta	300
atcgggcaaaa	tgtggagtgt	atgttctttt	cacagtaata	tatgcctttt	gtaacttcac	360
ttgggttattt	tattgtaaat	gaattacaaa	attcttaatt	taagaaaatg	gtangttata	420
tttanttcan	taatttcttt	ccttgtttac	gttaattttg	aaaagaatgc	at	472

&lt;210&gt; 96

&lt;211&gt; 476

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

35

&lt;222&gt; (1)...(476)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 96

ctgaagcatt	tcttcaaaact	tntctacttt	tgtcattgat	acctgtagta	agttgacaat	60
gtggtgaaat	ttcaaaaatta	tatgtaactt	ctactagttt	tactttctcc	cccaagtctt	120
ttttaactca	tgattttttac	acacacaatc	cagaacttat	tatatagcct	ctaagtcttt	180
attcttcaca	gtagatgatg	aaagagtcct	ccagtgtctt	gngcanaatg	ttctagntat	240
agctggatac	atacngtggg	agttctataa	actcatacct	cagtgggact	naaccaaaat	300
tgtgttagtc	tcaattccta	ccacactgag	ggagcctccc	aaatcactat	attcttatct	360
gcaggtactc	ctccagaaaa	acngacaggg	caggcttgca	tgaaaaagtn	acatctgcgt	420
tacaaagtct	atcttcctca	nangtctgtn	aaggaacaat	ttaatcttct	agcttt	476

&lt;210&gt; 97

&lt;211&gt; 479

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(479)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 97

actctttcta	atgctgatat	gatcttgagt	ataagaatgc	atatgtcact	agaatggata	60
aaataatgct	gcaaaactta	tgttcttatg	caaaatggaa	cgctaataga	acacagctta	120
caatcgcaaa	tcaaaaactca	caagtgtctca	tctgtttag	atttagtgta	ataagactta	180
gatttgctc	cttcggatat	gattgtttct	canatcttgg	gcaatnttcc	ttagtcaaat	240
caggctacta	gaattctggt	attggatatn	tgagagcatg	aaatttttaa	naatacactt	300
gtgattatna	aattaatcac	aaatttcact	tatacctgct	atcagcagct	agaaaaacat	360
ntnnttttta	natcaaagta	ttttgtgttt	ggaantgttn	aaatgaaatc	tgaatgtggg	420
ttcnactetta	ttttttcccn	gacnactant	tnctttttta	gggnctattc	tganccatc	479

&lt;210&gt; 98

&lt;211&gt; 461

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 98

agtgaattgt	cctccaacaa	aaccccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagttcc	tgtcatctat	tcgtacttaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttcctctac	ggatgagaga	ctggtcaag	aatatcctca	tgacgcttta	240
tgaagccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaaat	300
ttacctggag	aaaagaggct	ttggctgggg	accatcccat	tgaaccttct	cttaaggact	360
ttaagaaaaa	ctaccacatg	ttgtgtatcc	tggtgccggc	cgtttatgaa	ctgaccaccc	420
tttgaataaa	tcttgacgct	cctgaacttg	ctcctctgcg	a		461

&lt;210&gt; 99

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 99

gtggcgcgcg	gcaggtgttt	cctcgtaccg	cagggccccc	tcccttcccc	aggcgtccct	60
cggcgccctc	gcgggcccga	ggaggagcgg	ctggcggttg	gggggagtgt	gacccaccct	120
cggtgagaaa	agccttctct	agcgatctga	gaggcggtgc	ttgggggtac	c	171

<210> 100  
 <211> 269  
 <212> DNA  
 <213> Homo sapien

<400> 100  
 cgcccgcaag tgcaactcca gctggggcgcg tgcggacgaa gattctgccca gcagttggtc 60  
 cgactgcgac gacggcgccg ggcacagtcg caggtgcagc gcgggcgcct ggggtcttgc 120  
 aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga 180  
 cagccggaac agagcccggg gaagcgggag gcctcgggga gccctcggg aaggcgccgc 240  
 cgagagatac gcaggtgcag gtggccgcc 269

<210> 101  
 <211> 405  
 <212> DNA  
 <213> Homo sapien

<400> 101  
 tttttttttt ttttgaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca 60  
 gctagcaagg taacagggtg gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg 120  
 ttgattggtt tgcctttatg gggcgccggg ggggtagggg aaacgaagca aataacatgg 180  
 agtgggtgca ccctccctgt agaacctggt tacaagctt ggggcagttc acctggtctg 240  
 tgaccgtcat tttcttgaca tcaatgttat tagaagtcag gatattcttt agagagttcca 300  
 ctgttctgga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagttg 360  
 gatgatcagt acgaataccg aggcataattc tcatatcggg ggcca 405

<210> 102  
 <211> 470  
 <212> DNA  
 <213> Homo sapien

<400> 102  
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 <212> DNA  
 <213> Homo sapien

<400> 103  
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 <212> DNA  
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 <211> 1621  
 <212> DNA  
 <213> Homo sapien

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<210> 108  
 <211> 382  
 <212> PRT  
 <213> Homo sapien

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<400> 108
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35     40     45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50     55     60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65     70     75     80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85     90     95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100    105    110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115    120    125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130    135    140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145    150    155    160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165    170    175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180    185    190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195    200    205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg

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210	215	220
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Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala		255
	260	265
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp		270
	275	280
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val		285
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His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu		300
305	310	315
Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala		320
	325	330
Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu		335
	340	345
Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn		350
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<210> 109  
 <211> 1524  
 <212> DNA  
 <213> Homo sapien

<400> 109

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 <211> 3410  
 <212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 110

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<210> 111

<211> 1289

<212> DNA

<213> Homo sapien

<400> 111

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<210> 112

<211> 315

<212> PRT

<213> Homo sapien

<400> 112

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 Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu  
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 Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro  
 65 70 75 80  
 Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser  
 85 90 95  
 Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys  
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 Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe  
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 Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys  
 145 150 155 160



Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu  
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 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr  
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 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp  
 225 230 235 240  
 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val  
 245 250 255  
 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg  
 260 265 270  
 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly  
 275 280 285  
 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly  
 290 295 300  
 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp  
 305 310 315

&lt;210&gt; 113

&lt;211&gt; 553

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 113

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala  
 1 5 10 15  
 Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu  
 20 25 30  
 Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val  
 35 40 45  
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly  
 50 55 60  
 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly  
 65 70 75 80  
 Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile  
 85 90 95  
 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu  
 100 105 110  
 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly  
 115 120 125  
 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu  
 130 135 140  
 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala  
 145 150 155 160  
 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr  
 165 170 175  
 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu  
 180 185 190  
 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu  
 195 200 205  
 Thr Cys Val Ala Ala Thr Leu Val Ala Glu Glu Ala Ala Leu Gly  
 210 215 220  
 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His  
 225 230 235 240  
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu

245 250 255  
 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg  
 260 265 270  
 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe  
 275 280 285  
 Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val  
 290 295 300  
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 305 310 315 320  
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu  
 325 330 335  
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg  
 340 345 350  
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala  
 355 360 365  
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu  
 370 375 380  
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala  
 385 390 395 400  
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly  
 405 410 415  
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu  
 420 425 430  
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala  
 435 440 445  
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser  
 450 455 460  
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala  
 465 470 475 480  
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp  
 485 490 495  
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser  
 500 505 510  
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala  
 515 520 525  
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp  
 530 535 540  
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 545 550

&lt;210&gt; 114

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu  
 1 5 10 15  
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val  
 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile  
 85 90 95

Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met  
 130 135 140  
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp  
 145 150 155 160  
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn  
 165 170 175  
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala  
 180 185 190  
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile  
 195 200 205  
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly  
 210 215 220  
 Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu  
 225 230 235 240  
 Gln

<210> 115  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<400> 115  
 gctctttctc tccctctc tgaatttaat tctttcaact tgcaatttgc aaggattaca 60  
 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggt 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttaataaaat tagtttgggt 300  
 tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt 360  
 ttagtc 366

<210> 116  
 <211> 282  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(282)  
 <223> n = A,T,C or G

<400> 116  
 acaaagatga accatttcct atattatagc aaaattaaaa tctaccgta ttctaattatt 60  
 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120  
 agactttact attttcatat tttaagacac atgatttatc ctatttttagt aacctgggtc 180  
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240  
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<220>

45

<221> misc\_feature  
 <222> (1)...(305)  
 <223> n = A,T,C or G

<400> 117  
 acacatgtcg cttcactgcc ttcttagatg cttctgggtca acatanagga acagggacca 60  
 tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa 120  
 aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga 180  
 tactgatccc tgatcactgt cctaatagcag gatgtgggaa acagatgagg tcacctctgt 240  
 gactgcccc a gcttactgcc thtagagagt ttctangctg cagttcagac agggagaaat 300  
 tgggt 305

<210> 118  
 <211> 71  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(71)  
 <223> n = A,T,C or G

<400> 118  
 accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa 60  
 aantcctggg t 71

<210> 119  
 <211> 212  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(212)  
 <223> n = A,T,C or G

<400> 119  
 actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca 60  
 gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac 120  
 agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant 180  
 aatggantca aganactccc aggcctcagc gt 212

<210> 120  
 <211> 90  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(90)  
 <223> n = A,T,C or G

<400> 120  
 actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctttgcc 60  
 ctccgccggc gcagaacatg ctggggtgggt 90

<210> 121  
 <211> 218

<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(218)  
<223> n = A,T,C or G

<400> 121  
tgtancgtga anacgacaga naggggtgtc aaaaatggag aanccttgaa gtcattttga 60  
gaataagatt tgctaaaaga ttgggggcta aaacatgggt attgggagac atttctgaag 120  
atatncangt aaattangga atgaattcat gggtcttttg ggaattcctt tacgatngcc 180  
agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122  
<211> 171  
<212> DNA  
<213> Homo sapien

<400> 122  
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg 60  
catttggttag ctcatggaac aggaagtcgg atgggtggggc atcttcagtg ctgcatgagt 120  
caccaccccg gcggggtcat ctgtgccaca ggtcctgtt gacagtgcgg t 171

<210> 123  
<211> 76  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(76)  
<223> n = A,T,C or G

<400> 123  
tgtagcgtga agacnacaga atgggtgtgtg ctgtgctatc caggaaacaca tttattatca 60  
ttatcaanta ttgtgt 76

<210> 124  
<211> 131  
<212> DNA  
<213> Homo sapien

<400> 124  
acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt 60  
caatgtgtctg ggtcatatgg aggggaggag actctaaaat agccaatttt atttctcttg 120  
ttaagatttg t 131

<210> 125  
<211> 432  
<212> DNA  
<213> Homo sapien

<400> 125  
actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg 60  
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa 120  
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180  
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240

47

ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc	300
catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaattctcag	360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc	420
ctctttgctt gt	432

<210> 126  
 <211> 112  
 <212> DNA  
 <213> Homo sapien

<400> 126	
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat	60
agtaagaatg atatttcccc ccagggatca ccaaataattt ataaaaattt gt	112

<210> 127  
 <211> 54  
 <212> DNA  
 <213> Homo sapien

<400> 127	
accacgaaac cacaacaag atggaagcat caatccactt gccaagcaca gcag	54

<210> 128  
 <211> 323  
 <212> DNA  
 <213> Homo sapien

<400> 128	
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc	60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca	120
ttctctctga agtctagggtt acccattttg gggacccatt ataggcaata aacacagttc	180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt	240
ttcctgcaaa aggtcactc agtcctttgc ttgtcagtg gactgggctc ccagggcct	300
aggctgcctt cttttccatg tcc	323

<210> 129  
 <211> 192  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(192)  
 <223> n = A,T,C or G

<400> 129	
acatacatgt gtgtatattt ttaaataatca cttttgtatc actctgactt tttagcatac	60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc	120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg	180
gataaacaaa gt	192

<210> 130  
 <211> 362  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature

&lt;222&gt; (1)...(362)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 130

ccctttttta	tggaatgagt	agactgtatg	tttgaanatt	tanccacaac	ctctttgaca	60
tataatgacg	caacaaaaag	gtgctgttta	gtcctatggt	tcagtttatg	cccctgacaa	120
gtttccattg	tgttttgccg	atcttctggc	taatcgtggg	atcctccatg	ttattagtaa	180
ttctgtattc	cattttgtta	acgcctggta	gatgtaacct	gctangaggc	taactttata	240
cttattttaa	agctcttatt	ttgtggtcat	taaaatggca	atztatgtgc	agcactttat	300
tgcagcagga	agcacgtgtg	ggttggttgt	aaagctcttt	gctaattcta	aaaagtaatg	360
gg						362

&lt;210&gt; 131

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 131

ctttttgaaa	gatcgtgtcc	actcctgtgg	acatcttgtt	ttaatggagt	ttcccatgca	60
gtangactgg	tatggttgca	gctgtccaga	taaaaacatt	tgaagagctc	caaaatgaga	120
gttctccag	gttcgccctg	ctgtcccaag	tctcagcagc	agcctctttt	aggaggcatc	180
ttctgaacta	gattaaggca	gcttgtaa	ctgatgtgat	ttggtttatt	atccaactaa	240
cttccatctg	ttatcactgg	agaaagccca	gactcccan	gacnggtacg	gattgtgggc	300
atanaaggat	tgggtgaagc	tggcgttgtg	gt			332

&lt;210&gt; 132

&lt;211&gt; 322

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(322)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 132

acttttgcca	ttttgtatat	ataaacaatc	ttgggacatt	ctcctgaaaa	ctaggtgtcc	60
agtggctaag	agaactcgat	ttcaagcaat	tctgaaagga	aaaccagcat	gacacagaat	120
ctcaaattcc	caaacagggg	ctctgtggga	aaaatgaggg	aggacctttg	tatctcgggt	180
tttagcaagt	taaaatgaan	atgacaggaa	aggcttattt	atcaacaaag	agaagagttg	240
ggatgcttct	aaaaaaaaact	ttggtagaga	aaataggaat	gctnaatcct	agggaagcct	300
gtaacaatct	acaattggtc	ca				322

&lt;210&gt; 133

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 133

acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt	60
cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaacaac tctattgcta	120
ctatttaaaa aaaatcacia atctttccct ttaagctatg ttnaattcaa actattcctg	180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt	240
cccacgaaac actaataaaa accacagaga ccagcctg	278

&lt;210&gt; 134

&lt;211&gt; 121

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(121)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 134

gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca	60
tgattctctg aggttaaact tggttttcaa atgttatatt tacttgtatt ttgcttttgg	120
t	121

&lt;210&gt; 135

&lt;211&gt; 350

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(350)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 135

acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctatacc	60
atancaagtg gtgactgggt aagcgtgcga caaagggtcag ctggcacatt acttgtgtgc	120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca	180
gggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgt	240
ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgcctgag	300
ttccaagga tgcaaacct ggtgctcaac tcctggggcg tcaactcagt	350

&lt;210&gt; 136

&lt;211&gt; 399

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(399)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 136

tgtaccgtga agacgacaga agttgcatgg caggacaggg gcagggccga ggccagggtt	60
gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct	120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga	180
cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag	240
aaaactgcag aggccagggt tcagggtgna gtgggtangt gaccataaaa caccagggtgc	300
tcacagggaac ccgggcaaa gcatcctcca cctacagcca gcatgcccac tggcgtgatg	360
ggtgcagang gatgaagcag ccagntgttc tgctgtggt	399



50

<210> 137  
 <211> 165  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tnggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggctggtc ccaactggtg tcactgtcat tgggtggggt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120  
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180  
 tcatgtgttt ccagccacac caaaaggtgc ttgggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139  
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60  
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccga gtgaaggaga 120  
 attcaaacag acctcgatc tctggtgtg agcctggtcg gctcaccgcc tatcatctgc 180  
 atttgcccta ctcaggtgct accggactct ggcccctgat gtctgtagt tccacaggatg 240  
 ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat 300  
 gtcagctatg tgcccatcc tcttcatgc cctccctccc tttcctacca ctgctgagtg 360  
 gcctggaact tgtttaaagt gt 382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140  
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60  
 acttttctatt taacancttt tggttaagtgt caggctgcac ttgctccat anaattattg 120  
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180  
 atattcagca taaaggagaa 200

<210> 141  
 <211> 335  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(335)  
 <223> n = A,T,C or G

<400> 141  
 actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60  
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt 120  
 atgcatgtag agaaccctaa ctaattttatt aaacaggata gaaacaggct gtctgggtga 180  
 aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240  
 tttttctacc agttcagaga tnggttaatg actantcca atggggaaaa agcaagatgg 300  
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142  
 <211> 459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(459)  
 <223> n = A,T,C or G

<400> 142  
 accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60  
 ggggttgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120  
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180  
 cacatggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc 240  
 ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca 300  
 tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360  
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420  
 cagcangggg gggaggaacc agctcaacct tggcgtant 459

<210> 143  
 <211> 140  
 <212> DNA  
 <213> Homo sapien

<400> 143  
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60  
 aaatccaaac agtctctcct agaaaggaat agtgtacca accccaccca tctccctgag 120  
 accatccgac ttccctgtgt 140

<210> 144  
 <211> 164  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(164)  
 <223> n = A,T,C or G

<400> 144  
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60  
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta taaaaatttg 120  
 aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt 164

<210> 145  
 <211> 303  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 145  
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60  
 actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctccaggctat 120  
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180  
 gtaggggagt ccattccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240  
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300  
 caa 303

<210> 146  
 <211> 327  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(327)  
 <223> n = A,T,C or G

<400> 146  
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60  
 actggccttg agtgactcat tgctctggtt ggttgagaga gtcctttgc caacaggcct 120  
 ccaagtcagg gctgggattt gtttccttcc cacattctag caacaatatg ctggccactt 180  
 cctgaacagg gaggggtgga ggagccagca tggacaagc tgccactttc taaagtagcc 240  
 agacttgccc ctgggcctgt cacacctact gatgacctc tgtgcctgca ggatggaatg 300  
 taggggtgag ctgtgtgact ctatggt 327

<210> 147  
 <211> 173  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(173)  
 <223> n = A,T,C or G

<400> 147

acattgtttt	tttgagataa	agcattgana	gagctctcct	taacgtgaca	caatggaagg	60
actggaacac	ataccacat	ctttgttctg	agggataatt	ttctgataaa	gtcttgctgt	120
atattcaagc	acatatgtta	tatattattc	agttccatgt	ttatagccta	ggt	173

&lt;210&gt; 148

&lt;211&gt; 477

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(477)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 148

acaaccactt	tatctcatcg	aatttttaac	ccaaactcac	tcactgtgcc	tttctatcct	60
atgggatata	ttatttgatg	ctccatttca	tcacacatat	atgaataata	cactcatact	120
gccctactac	ctgctgcaat	aatcacattc	ccttctctgc	ctgaccctga	agccattggg	180
gtgggtcctag	tggccatcag	tccangcctg	caccttgagc	ccttgagctc	cattgctcac	240
nccanccac	ctaccgacc	ccatcctctt	acacagctac	ctccttgctc	tctaacccca	300
tagattatnt	ccaaattcag	tcaattaagt	tactattaac	actctaccg	acatgtccag	360
caccactggg	aagccttctc	cagccaacac	acacacacac	acacncacac	acacacatat	420
ccaggcacag	gctacctcat	cttcacaatc	acccctttaa	ttaccatgct	atgggtgg	477

&lt;210&gt; 149

&lt;211&gt; 207

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 149

acagttgtat	tataatatca	agaaataaac	ttgcaatgag	agcatttaag	agggagaagc	60
taacgtatnt	tagagagcca	aggaagggtt	ctgtggggag	tgggatgtaa	ggtggggcct	120
gatgataaat	aagagtcagc	caggtaagtg	ggtggtgtgg	tatgggcaca	gtgaagaaca	180
tttcaggcag	aggaacagc	agtgaaa				207

&lt;210&gt; 150

&lt;211&gt; 111

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(111)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 150

accttgattt	cattgctgct	ctgatggaaa	cccaactatc	taatttagct	aaaacatggg	60
cacttaaatg	tggtcagtg	ttggacttgt	taactantgg	catctttggg	t	111

&lt;210&gt; 151

&lt;211&gt; 196

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 151

agcgcgag	gtcatattga	acattccaga	tacctatcat	tactcgatgc	tggtgataac	60
agcaagatgg	ctttgaactc	agggtcacca	ccagctattg	gaccttacta	tgaaaaccat	120
ggataccaac	cggaaaaccc	ctatcccgc	cagcccactg	tggtccccc	tgtctacgag	180

gtgcatccgg ctcaagt

196

&lt;210&gt; 152

&lt;211&gt; 132

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 152

acagcacttt cacatgtaag aaggagaaaa ttctaaatg taggagaaag ataacagAAC 60  
 cttccccctt tcatctagt gtggaaacct gatgctttat gttgacagga atagaaccag 120  
 gagggagttt gt 132

&lt;210&gt; 153

&lt;211&gt; 285

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(285)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 153

acaanaccCA nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag 60  
 cttctgtctt tatgtcctca tctgacaact ctttaccatt ttatcctcg ctCagcagga 120  
 gcacatcaat aaagtccaaa gtcttggaact tggccttggc ttggagggaag tcatcaacac 180  
 cctggctagt gaggggtgcg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca 240  
 gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt 285

&lt;210&gt; 154

&lt;211&gt; 333

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 154

accacagtcc tgttggggcca gggcttcatg accctttctg tgaaaagcca tattatcacc 60  
 accccaaatt ttctcttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac 120  
 cctaagccgg ttacacagct aactcccaact ggccctgatt tgtgaaattg ctgctgcctg 180  
 attggcacag gagtgcgaagg tgttcagctc ccctcctccg tggaaacgaga ctctgatttg 240  
 agtttcacaa attctcgggc cacctcgtca ttgtcctct gaaataaaat ccggagaatg 300  
 gtcaggcctg tctcatccat atggatcttc cgg 333

&lt;210&gt; 155

&lt;211&gt; 308

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(308)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 155

actggaaata ataaaaccCA catcacagt tttgttcaaa gatcatcagg gcatggatgg 60  
 gaaagtgttt tgggaactgt aaagtgccta acacatgac gatgattttt gttataatat 120  
 ttgaatcag gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc 180  
 atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggt 240  
 gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtga aggcagctg 300

gccctggt

308

<210> 156  
 <211> 295  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 156

accttgctcg	gtgcttgga	catattagga	actcaaaata	tgagatgata	acagtgccta	60
ttattgatta	ctgagagaac	tgtagacat	ttagttgaag	attttctaca	caggaactga	120
gaataggaga	ttatgtttg	ccctcatatt	ctctcctatc	ctccttgctt	cattctatgt	180
ctaataatatt	ctcaatcaaa	taaggttagc	ataatcagga	aatcgaccaa	ataccaatat	240
aaaaccagat	gtctatcctt	aagattttca	aatagaaaac	aaattaacag	actat	295

<210> 157  
 <211> 126  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 157

acaagtttaa	atagtgtgt	cactgtgcat	gtgctgaaat	gtgaaatcca	ccacatttct	60
gaagagcaaa	acaaattctg	tcatgtaatc	tctatcttgg	gtcgtgggta	tatctgtccc	120
cttagt						126

<210> 158  
 <211> 442  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(442)  
 <223> n = A,T,C or G

&lt;400&gt; 158

accactggt	cttggaaca	cccatcctta	atacgatgat	ttttctgtcg	tgtgaaaatg	60
aanccagcag	gctgccccta	gtcagtcctt	ccttccagag	aaaaagagat	ttgagaaagt	120
gcctgggtaa	ttcaccatta	atttcctccc	ccaaactctc	tgagtcttcc	cttaatatatt	180
ctgggtgggtc	tgaccaaagc	aggtcatggt	ttgttgagca	tttgggatcc	cagtgaagta	240
natgtttgta	gccttgcata	cttagccctt	cccacgcaca	aacggagtgg	cagagtgggtg	300
ccaaccctgt	tttcccagtc	cacgtagaca	gattcacagt	gcggaattct	ggaagctgga	360
nacagacggg	ctctttgcag	agccgggact	ctgagangga	catgagggcc	tctgcctctg	420
tgttcattct	ctgatgtcct	gt				442

<210> 159  
 <211> 498  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(498)  
 <223> n = A,T,C or G

&lt;400&gt; 159

acttccaggt	aacgttgttg	tttccgttga	gcctgaactg	atgggtgacg	ttgtaggttc	60
tccaacaaga	actgagggtg	cagagcgggt	aggggaagagt	gctgttccag	ttgcacctgg	120
gctgctgtgg	actgttgttg	attcctcact	acggcccaag	gttgtggaac	tggcanaaag	180

```

gtgtgttgtt ggantttagc tcgggcggct gtggtaggtt gtgggtctt caacaggggc 240
tgctgtggtg ccgggangtg aangtggtgt gtcacttgag cttggccagc tctggaaagt 300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa 360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn 420
tcaggttaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc 480
aagggaataa gctgtggt 498

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac 60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct 120
ggagcatggc atagagggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc 180
cactagacat ctcatcagcc acttggtgta agagatgcc catgaccca gatgcctctc 240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg 300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa 360
ctttagaat gaagcctgga 380

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttgcc ttgcctgtca 60
cactgtccac tggccctta tccacttggt gcttaatccc tcgaaagagc atgt 114

```

```

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

```

```

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa 60
gttttactac tctgataatt ttgtaacca ggtaaccaga acatccagtc atacagcttt 120
tggatgata taacttgga ataaccagc ctggtgatac ataaaactac tcactgt 177

```

```

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(137)
<223> n = A,T,C or G

```

```

<400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac 60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt 120

```

catcagcggc atgatgt

137

&lt;210&gt; 164

&lt;211&gt; 469

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(469)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 164

cttatcacia	tgaatgttct	cctgggcagc	gttgtgatct	ttgccacctt	cgtgacttta	60
tgcaatgcat	catgctat	cataccta	gagggagttc	caggagattc	aaccaggaaa	120
tgcatggatc	tcaaaggaaa	caaacacca	ataaactcgg	agtggcagac	tgacaactgt	180
gagacatgca	cttgctacga	aacagaaatt	tcatgttgca	cccttgtttc	tacacctgtg	240
ggttatgaca	aagacaactg	ccaagaatc	ttcaagaagg	aggactgcaa	gtatatcgtg	300
gtggagaaga	aggacccaaa	aaagacctgt	tctgtcagtg	aatggataat	ctaattgtgt	360
tctagtaggc	acagggctcc	caggccaggc	ctcattctcc	tctggcctct	aatagtcaat	420
gattgtgtag	ccatgcctat	cagtaaaaag	atntttgagc	aaacacttt		469

&lt;210&gt; 165

&lt;211&gt; 195

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(195)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 165

acagtttttt	atanatatcg	acattgccgg	cacttgtgtt	cagtttcata	aagctgggtg	60
atccgctgtc	atccactatt	ccttggttag	agtaaaaatt	attcttatag	cccatgtccc	120
tgaggccgc	ccgccgtag	ttctcgttcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tcctctgaga	tgagt					195

&lt;210&gt; 166

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgaggtcggg	gtccacacca	ccggtgtagg	tgtgtcfaat	cttgggcttg	gcgcccacct	120
ttggagaagg	gatatgctgc	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgagacc	agcctgagca	aggggcggat	gttcagcttc	agctcctcct	tcgtcagggtg	240
gatgccaaac	tcgtctangg	tccgtgggaa	gctgggtgtc	acntcaccta	caacctgggc	300
gangatctta	taaaggaggt	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360
nggggccttt	ttggtgaact	ttc				383

&lt;210&gt; 167



<211> 247  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167  
 acagagccag accttgccca taaatgaanc agagattaag actaaacccc aagtcganat 60  
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120  
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180  
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240  
 tgangtc 247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168  
 acttctaagt ttcttagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60  
 aatccctcan ccttgttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg 120  
 gctgacacct gagcctgnat tttactcat ccctgagaag ccctttccag taggggtggc 180  
 aattccaac ttcccttgcca caagcttccc aggctttctc ccctggaaaa ctccagcttg 240  
 agtcccagat acactcatgg gctgcccctgg gca 273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169  
 acagccttgg ctccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60  
 agctcagacc aggggtcaaa gatgtgacat caacagtttc tggtttcaga acaggttcta 120  
 ctactgtcaa atgaccccc atacttctc aaaggctgtg gtaagttttg cacaggtgag 180  
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240  
 cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tctactgctgg gcaccagctc 300  
 acgcacatca ctgacaaccg ggatggaaaa agaantgcc aactttcatac atccaactgg 360  
 aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420  
 tcgaacactg a 431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

59

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

<400> 170  
 acctgtgggc tgggctgtta tgccctgtgcc ggctgctgaa agggagttca gaggtggagc 60  
 tcaaggagct ctgcaggcat ttgccaanc ctctccanag canagggagc aacctacact 120  
 ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat 180  
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240  
 tcaaagctag gggctctggca ggtgga 266

<210> 171  
 <211> 1248  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1248)  
 <223> n = A,T,C or G

<400> 171  
 ggcagccaaa tcataaacgg cgaggactgc agcccgact cgcagccctg gcaggcggca 60  
 ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcattccga gtgggtgctg 120  
 tcagccgcac actgtttcca gaagtgtgtg cagagctcct acaccatcgg gctgggcctg 180  
 cacagtcttg aggcggacca agagccaggg agccagatgg tggaggccag cctctccgta 240  
 cggcaccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac 300  
 gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc 360  
 gcggggaaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc 420  
 gtgctgcagt gcgtgaacgt gtcggtgggtg tctgaggagg tctgcagtaa gctctatgac 480  
 ccgctgtacc accccagcat gttctgcgcc ggccggaggcg aagaccagaa ggactcctgc 540  
 aacgggtgact ctggggggcc cctgatctgc aacgggtact tgcaaggcct tgtgtctttc 600  
 ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc 660  
 actgagtggg tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa 720  
 attgaccccc aaatacatcc tgcggaagga attcaggaa atctgttccc agccccctcct 780  
 ccctcaggcc caggagtcca ggccccagc ccctcctccc tcaaaccaag ggtacagatc 840  
 ccagccctc cctccctcag acccaggagt ccagacccc cagccctcc tccctcagac 900  
 ccaggagtcc agccccctc cctcagacc caggagtcca gacccccag cccctcctcc 960  
 ctcagaccca ggggtccagg cccccaaccc ctccctccctc agactcagag gtccaagccc 1020  
 ccaaccntc attccccaga cccagaggtc cagggtccag ccctcntcc ctcagaccca 1080  
 gcggtccaat gccacctaga ctntccctgt acacagtgcc cccttggtgc acgttgaccc 1140  
 aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt 1200  
 aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1248

<210> 172  
 <211> 159  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(159)  
 <223> Xaa = Any Amino Acid

<400> 172  
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro  
 1 5 10 15

Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser  
 20 25 30  
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr  
 35 40 45  
 Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly  
 50 55 60  
 Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu  
 65 70 75 80  
 Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe  
 85 90 95  
 Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser  
 100 105 110  
 Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe  
 115 120 125  
 Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn  
 130 135 140  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 145 150 155

&lt;210&gt; 173

&lt;211&gt; 1265

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1265)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 173

```

ggcagccgcg actgcagcc ctggcaggcg gcaactggtca tggaaaacga attgttctgc      60
tcgggcgtcc tgggtgcaccc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc      120
tacaccatcg ggctgggcct gcacagtctt gaggcgacc aagagccagg gagccagatg      180
gtggaggcca gcctctccgt acggcaccca gactacaaca gaccttgtct cgctaacgac      240
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc      300
attgcttcgc agtgccctac cgcggggaac tcttgctctg tttctggctg ggtctgtctg      360
gcgaacgggt agctcacggg tgtgtgtctg cctcttcaa ggaggtcctc tgcccagtcg      420
cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga      480
acgtgtcggg ggtgtctgag gaggtctgca gtaagctcta tgaccgctg taccaccca      540
gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg      600
ggccctgat ctgcaacggg tacttgagcag gccttggtgc tttcgaaaaa gcccctgtg      660
gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga      720
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac      780
atcctgcgga aggaattcag gaatatctgt tcccagcccc tctcctca ggcccaggag      840
tccaggcccc cagccctcc tccctcaaac caagggtaca gatccccagc cctcctccc      900
tcagaccagc gagtccagac cccccagccc ctctccctc agacccagga gtccagcccc      960
tctcctntca gaccaggag tccagacccc ccagcccctc ctccctcaga cccagggggt      1020
gaggcccca accctcctc cttcagagtc agaggtccaa gcccacaacc cctcgttccc      1080
cagaccagga ggttnaggtc ccagcccctc ttcctcaga cccagnngtc caatgccacc      1140
tagattttcc ctgnacacag tgcccccttg tggngangttg acccaacott accagttggt      1200
ttttcatttt tngtcccttt ccctagatc cagaaataaa gtttaagaga ngngcaaaaa      1260
aaaaa
  
```

&lt;210&gt; 174

&lt;211&gt; 1459

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1459)  
 <223> n = A,T,C or G

<400> 174

ggtcagccgc	acactgtttc	cagaagtgc	tgacagctc	ctacaccatc	gggctgggccc	60
tgacagctc	tgaggccgac	caagagccag	ggagccagat	ggaggaggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgctc	atcaagttgg	180
acgaatccgt	gtccgagctc	gacaccatcc	ggagcatcag	cattgcttcg	cagtgcctta	240
ccgcggggaa	ctcttgccct	gtttctggct	gggtctgct	ggcgaacggg	gagctcacgg	300
gtgtgtgtc	gccctcttca	aggaggtcct	ctgccagtc	gcgggggctg	acccagagct	360
ctgcgtccca	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tggtgtctga	420
ngaggtctgc	antaagctct	atgaccgct	gtaccacccc	ancatgttct	gcgccggcgg	480
agggcaagac	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
caggggaagg	tggaagagg	ggagacagag	acacacaggg	ccgcattggc	agatgcagag	600
atggagagac	acacagggag	acagtgcaca	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaagga	agagagaaac	agaaacagac	atggggaggc	720
agaaacacac	acacatagaa	atgcagttga	ccttccaaca	gcattggggc	tgaggcggt	780
gacctccacc	caatagaaaa	tcctcttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtcgattt	atgcatacgt	900
tttatgcatt	catgatatac	ctttgttga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	ttttttaaat	tggtgcaact	ctcctaaaa	ttttctgatg	tggttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaaccagg	gttgttcaag	ggtcaactgt	1080
gtaccacagag	ggaacacagt	acacagattc	atagaggtga	aacacgaaga	gaaacaggaa	1140
aatcaagac	tctacaaaga	ggctgggcag	ggtggctcat	gcctgtaatc	ccagcacttt	1200
gggagggcag	gcaggcagat	cacttgaggt	aaggagttca	agaccagcct	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatgggtgg	aggcgctgt	1320
aatcccagct	acttgggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagagggt	1380
gaagtgcgtt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaa					1459

<210> 175  
 <211> 1167  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1167)  
 <223> n = A,T,C or G

<400> 175

gcgcagccct	ggcaggcgcc	actggtcatg	gaaaacgaat	tggtctgctc	gggcgtcctg	60
gtgcacccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	180
ctctccgtac	ggcaccacaga	gtacaacaga	ctcttgctcg	ctaaccgacct	catgctcatc	240
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcatacagcat	tgcttcgcag	300
tgccctaccg	cggggaactc	ttgcctcgtn	tctggctggg	gtctgctggc	gaacggcaga	360
atgcctaccg	tgctgcaactg	cgtgaacgtg	tcggtggtgt	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcccgc	gcggagggca	agaccagaag	480
gactcctgca	acggtgactc	tgggggggccc	ctgatctgca	acgggtactt	gcagggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgtgc	caggtgtcta	caccaacctc	600
tgcaaatcca	ctgagtggtg	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgaccccca	aatacatcct	gcggaangaa	ttcaggaata	tctgttccca	720
gcccctcctc	cctcaggccc	aggagtccag	gccccagcc	cctcctccct	caaaccaagg	780
gtacagatcc	ccagcccctc	ctccctcaga	cccaggagtc	cagaccccc	agcccctcnt	840
ccntcagacc	caggagtcca	gcccctcctc	cntcagacgc	aggagtccag	accccccagc	900

```

ccntcntccg tcagaccag ggtgcaggc ccccaacccc tcntccntca gagtcagagg      960
tccaagcccc caaccctcg tccccagac ccagaggtnc aggtcccagc cctcctccc      1020
tcagaccag cggtccaatg ccacctagan tntccctgta cacagtgcc cttgtggca      1080
ngttgaccca acctaccag ttggtttttc atttttgtc cttttccct agatccagaa      1140
ataaagtnta agagaagcgc aaaaaaa      1167

```

<210> 176  
 <211> 205  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(205)  
 <223> Xaa = Any Amino Acid

```

<400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
 50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
100          105          110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
115          120          125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
130          135          140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
145          150          155          160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
165          170          175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
180          185          190
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
195          200          205

```

<210> 177  
 <211> 1119  
 <212> DNA  
 <213> Homo sapien

```

<400> 177
gcgcactcgc agccctggca ggcggcactg gtcattgaaa acgaattggt ctgctcgggc      60
gtcctgtgtc atccgcagt ggtgctgtca gccgcacact gttccagaa ctcctacacc      120
atcgggctgg gctgcacag tcttgaggcc gaccaagagc caggagcca gatggtggag      180
gccagcctct ccgtacggca cccagagtag aacagaccct tgctcgctaa cgacctcatg      240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct      300
tcgcagtgcc ctaccgagg gaaactcttg ctcgtttctg gctgggtct gctggcgaac      360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc      420
caaccctggc aggggtgtac catttcggca acttccagt caaggacgtc ctgctgcatc      480

```

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ctcactgggt gctcactact gctcactgca tcaccoggaa cactgtgata aactagccag 540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
actaaccatg cccgatgtta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
cagttatcct cactgaattg agatttctctg cttcagtgtc agccattccc acataatttc 720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtagtc ccctcacaaa 780
ttcatttctc ctgtttagt gaaagggtgc ccctctggag cctcccaggg tgggtgtgca 840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg 900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca 960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg 1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc 1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaa 1119

```

&lt;210&gt; 178

&lt;211&gt; 164

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(164)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
100         105         110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
115         120         125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
130         135         140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Thr Ala Ser
145         150         155         160
Pro Gly Thr Leu

```

&lt;210&gt; 179

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 179

```

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct 120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga 180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa 240
aaaaaaaaa
250

```

64

<210> 180  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<400> 180  
 actagtccag tgggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca 60  
 tcacccagac cccgcccctg cccgtgcccc acgtgctgc taacgacagt atgatgctta 120  
 ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc 180  
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181  
 <211> 558  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(558)  
 <223> n = A,T,C or G

<400> 181  
 tccytttght naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60  
 aatgttttagg cagtgttagt aatttcytcg taatgattct gttattactt tcctnattct 120  
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180  
 ggtagtgtag tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240  
 aaattatgca agttagtaat tactcagggg taactaaatt actttaatat gctgttgaac 300  
 ctactctgtt ccttggttag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360  
 attgataata ttctatgttc taaaagttag gctatacata aattattaag aaatatggaw 420  
 ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480  
 aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540  
 caaaaaaaaa aaaaaaaaaa 558

<210> 182  
 <211> 479  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(479)  
 <223> n = A,T,C or G

<400> 182  
 acagggwttk grggatgcta agsccccrga rwtggtttga tccaaccctg gcttwttttc 60  
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120  
 cstcacacag astcccagat agctgggact acaggcacac agtcactgaa gcaggccctg 180  
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240  
 ctaaggttta actttccac ccagaaaagg caacttagat aaaatcttag agtactttca 300  
 tactmttcta agtcctcttc cagcctcact kkgagtcctm cytggggggt gataggaant 360  
 ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttg tacycatara 420  
 awtgstgara aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 183

aggcgggagc	agaagctaaa	gccaaagccc	aagaagagt	gcagtgccag	cactgggtgcc	60
agtaccagta	ccaataacag	tgccagtgcc	agtgccagca	ccagtgggtg	cttcagtgtc	120
ggtgccagcc	tgaccgccac	tctcacattt	gggtctctcg	ctggccttgg	tgagctgggt	180
gccagcacca	gtggcagctc	tggtgcctgt	ggtttctcct	acaagtgaga	ttttagatat	240
tgtaatcct	gccagtcttt	ctctcaagc	caggggtgcat	cctcagaaac	ctactcaaca	300
cagcactcta	ggcagccact	atcaatcaat	tgaagttgac	actctgcatt	aratctattt	360
gccatttcaa	aaaaaaaaaa	aaaa				384

&lt;210&gt; 184

&lt;211&gt; 496

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(496)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 184

accgaattgg	gaccgctggc	ttataagcga	tcatgtyynt	ccrgtatcac	ctcaacgagc	60
aggagatcgc	agtctatacg	ctgaagaaat	ttgaccgat	gggacaacag	acctgctcag	120
cccatcctgc	tcggttctcc	ccagatgaca	aatactctsg	acaccgaatc	accatcaaga	180
aacgcttcaa	ggtgctcatg	accagcaac	cgcgcctgt	cctctgaggg	tcccttaaac	240
tgatgtcttt	tctgccacct	gttaccctc	ggagactccg	taaccaaact	cttcggactg	300
tgagccctga	tgctttttg	ccagccatac	tctttggcat	ccagtctctc	gtggcgattg	360
attatgcttg	tgtgaggcaa	tcatggtggc	atcacccata	aagggaacac	atttgacttt	420
tttttctcat	attttaaatt	actacmagaw	tattwmagaw	waaatgawtt	gaaaaactst	480
taaaaaaaaa	aaaaaa					496

&lt;210&gt; 185

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 185

gctggtagcc	tatggcgkcg	cccacggagg	ggctcctgag	gccacggrac	agtgacttcc	60
caagtatcyt	gcgcsgcgtc	ttctacogtc	cctacctgca	gatcttcggg	cagattcccc	120
aggaggacat	ggacgtggcc	ctcatggagc	acagcaactg	ytcgtcggag	cccggcttct	180
gggcacaccc	tcctggggcc	caggcgggca	cctgcgtctc	ccagtatgcc	aactggctgg	240
tggtgctgct	cctcgtcatc	ttcctgctcg	tggccaacat	cctgctggtc	aacttgctca	300
ttgccatggt	cagttacaca	ttcggcaaa	tacagggcaa	cagcgatctc	tactgggaag	360
gcgcagcgtt	accgcctcat	ccgg				384

&lt;210&gt; 186

&lt;211&gt; 577

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(577)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 186

gagttagctc	ctccacaacc	ttgatgaggt	cgtctgcagt	ggcctctcgc	ttcataccgc	60
tnccatcgtc	atactgtagg	tttgccacca	cytcctggca	tcttggggcg	gcntaatatt	120
ccaggaaact	ctcaatcaag	tcaccgtcga	tgaaacctgt	gggctgggtc	tgtcttcgcg	180



```

tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgacttt      240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac      300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaagt      360
ctcaccacaga ttctgcatta ccagagagcc gtggcaaaag acattgacaa actcgcccag      420
gtggaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgttggt ggcagcgctw      480
tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcatcatcc      540
aagatntcgc acagcactna tccagttggg attaaat                                577

```

&lt;210&gt; 187

&lt;211&gt; 534

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(534)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 187

```

aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaaticatw      60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact      120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggtg      180
tgccctatcc acacctgtta aaaggcgctt aagcattttt gattcaacat cttttttttt      240
gacacaaagtc cgaaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc      300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttggyggagc      360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg      420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg      480
aggatctccc agtttattta ccacttgcac aagaaggcgt tttcttcctc aggc                                534

```

&lt;210&gt; 188

&lt;211&gt; 761

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(761)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 188

```

agaaaccagt atctctnaaa acaacctctc ataccttggt gacctaatTT tgtgtgcgtg      60
tgtgtgtgog cgcataattat atagacaggc acatcttttt tacttttgta aaagcttatg      120
cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaagtgt actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg      300
ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa      360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt      420
gcaaaaaaca tgtacngact tcccgttgag taatgccaag ttgttttttt tatnataaaa      480
cttgcccttc attacatggt tnaaagtggg gtgggtgggc aaaatattga aatgatggaa      540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac      600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta      660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac      720
gaaaataata acattgaaga aaaaanaaaa aanaaaaaaa a                                761

```

&lt;210&gt; 189

&lt;211&gt; 482

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

67

<220>  
 <221> misc\_feature  
 <222> (1)...(482)  
 <223> n = A,T,C or G

<400> 189  
 tttttttttt tttgccgatn ctactatntt attgcaggan gtgggggtgt atgcaccgca 60  
 caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120  
 aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc 180  
 aaggcagggg ccaccagtcc aggggtggga atacagggg tgggangtgt gcataagaag 240  
 tgataggcac aggccacccg gtacagaccc ctgggtcctt gacaggtnga tttcgaccag 300  
 gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc 360  
 aaatttggct ngtcattngaa ngggcanttt tccaanttng gctnngtctt ggtacncttg 420  
 gttcggccca gctccnctgc caaaaantat tcacccnctt ccnaattgct tgcnggnccc 480  
 cc 482

<210> 190  
 <211> 471  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(471)  
 <223> n = A,T,C or G

<400> 190  
 tttttttttt ttttaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg 60  
 aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtntctcca 120  
 aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180  
 cgcttttgac atacaatgca caaaaaaaa aggggggggg gaccacatgg attaaaattt 240  
 taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300  
 tgaaaaattt catgtatgca atccaaccaa agaacttnat tggtagatcat gantnctcta 360  
 ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacnctgt acaaaaanaa 420  
 tctgtaattn anttcaacct ccgtacngaa aaatntntnt tatacactcc c 471

<210> 191  
 <211> 402  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(402)  
 <223> n = A,T,C or G

<400> 191  
 gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60  
 gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120  
 attcttcacc agtcacatct tctaggacct ttttgattc agttagtata agctcttcca 180  
 cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg 240  
 ctcggtctct aacaatgtcc tctccttgaa gtatttggct gaacaacca cctaaagtcc 300  
 ctttgtcat ccatttttaa tatacttaat agggcattgk tncactaggt taaattctgc 360  
 aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca 402

<210> 192  
 <211> 601

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(601)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 192

gagctcggat	ccaataatct	ttgtctgagg	gcagcacaca	tatncagtgc	catggnaact	60
ggtctacccc	acatgggagc	agcatgccgt	agntatataa	ggtcattccc	tgagtcagac	120
atgcytyttt	gaytaccgtg	tgccaagtgc	tggtgattct	yaacacacyt	ccatcccgyt	180
cttttgtgga	aaaactggca	cttktctgga	actagcarga	catcacttac	aaattcaccc	240
acgagacact	tgaaggtgt	aacaaagcga	ytcttgcat	gctttttgtc	cctccggcac	300
cagttgtcaa	tactaaccog	ctggtttgcc	tccatcacat	ttgtgatctg	tagctctgga	360
tacatctcct	gacagtactg	aagaacttct	tcttttgttt	caaaagcarg	tcttggtgcc	420
tgttggatca	ggttcccatt	tcccagtcyg	aatgttcaca	tgcatattt	wacttccac	480
aaaacattgc	gatttgaggc	tcagcaacag	caaatcctgt	tcgggcattg	gctgcaagag	540
cctcgatgta	gccggccagc	gccaaaggcag	gcgccgtgag	ccccaccagc	agcagaagca	600
g						601

&lt;210&gt; 193

&lt;211&gt; 608

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(608)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 193

atacagccca	natcccacca	cgaagatgcg	cttggtgact	gagaacctga	tgcggtcact	60
ggtcccgtg	tagccccagc	gactctccac	ctgctggaag	cggttgatgc	tgactctytt	120
cccaacgcag	gcagmagcgg	gscgggtcaa	tgaactccay	tcgtggcttg	gggtkgacgg	180
tkaagtgcag	gaagaggctg	accacctcgc	ggteccaccag	gatgcccagc	tgtcggggac	240
ctgcagcgaa	actcctcgat	ggtcatgagc	gggaagcgaa	tgaggcccag	ggccttgccc	300
agaaccttcc	gcctgttctc	tggcgtcacc	tgagctgct	gccgctgaca	ctcggcctcg	360
gaccagcgga	caaacggcrt	tgaacagccg	cacctcacgg	atgcccagtg	tgtcgcgctc	420
caggammgsc	accagcgtgt	ccaggtcaat	gtcgggtgaag	ccctccgcgg	gtratggcgt	480
ctgcagtgtt	tttgtcgatg	ttctccaggc	acaggctggc	cagctgcggg	tcacggaaga	540
gtcgcgctg	cgtgagcagc	atgaaggcgt	tgtcggtctg	cagttcttct	tcaggaactc	600
cacgcaat						608

&lt;210&gt; 194

&lt;211&gt; 392

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(392)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 194

gaacggctgg	accttgccctc	gcattgtgct	tgctggcagg	gaataccttg	gcaagcagyt	60
ccagtcagg	cagccccaga	ccgtgcccgc	ccgaagctaa	gcctgcctct	ggccttcccc	120
tccgcctcaa	tgacagaacca	gtagtgggag	cactgtgttt	agagttaaga	gtgaacactg	180

tttgatttta	cttgggaatt	tcctctgtta	tatagctttt	cccaatgcta	atttccaaac	240
aacaacaaca	aaataacatg	tttgccctgtt	aagttgtata	aaagtaggtg	attctgtatt	300
taaagaaaat	attactgtta	catatactgc	ttgcaatttc	tgtattttatt	gktnctstgg	360
aaataaatat	agttattaaa	ggttgtcant	cc			392

&lt;210&gt; 195

&lt;211&gt; 502

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(502)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 195

ccsttkgagg	ggtkaggkyc	cagttyccga	gtggaagaaa	caggccagga	gaagtgcgtg	60
ccgagctgag	gcagatgttc	ccacagtgc	ccccagagcc	stgggstata	gtytctgacc	120
cctcncaagg	aaagaccacs	ttctggggac	atgggctgga	gggcaggacc	tagaggcacc	180
aagggaaggg	cccattcccg	ggstgttccc	cgaggaggaa	gggaaggggc	tctgtgtgcc	240
ccccasgagg	aagaggccct	gagtcctggg	atcagacacc	ccttcacgtg	tatccccaca	300
caaatgcaag	ctcaccaagg	tcccctctca	gtccccttcc	stacaccctg	amcggccact	360
gscscacacc	cacccagagc	acgccaccgg	ccatggggar	tgtgctcaag	gartcgcnng	420
gcarcgtgga	catctngtcc	cagaaggggg	cagaatctcc	aatagangga	ctgarcmstt	480
gctnanaaaa	aaaaanaaaa	aa				502

&lt;210&gt; 196

&lt;211&gt; 665

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(665)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 196

ggttacttgg	tttcattgcc	accacttagt	ggatgtcatt	tagaaccatt	ttgtctgctc	60
cctctggaag	ccttgccgag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	120
wagctgtttk	gagttgatts	gcaccactgc	accacaact	tcaatatgaa	aacyawttga	180
actwatttat	tatcttgtga	aaagtataac	aatgaaaatt	ttgttcatac	tgtattkatc	240
aagtatgatg	aaaagcaawa	gatataat	cttttattat	gttaaattat	gattgccatt	300
attaatcggc	aaaatgtgga	gtgtatgttc	ttttcacagt	aatatatgcc	ttttgtaact	360
tcacttgggt	attttattgt	aaatgartta	caaaattctt	aatttaagar	aatgggtatgt	420
watatattatt	tcattaattt	ctttcctkgt	ttacgtwaat	tttgaaaaga	wtgcatgatt	480
tcttgacaga	aatcgatctt	gatgctgtgg	aagtagtttg	accacatoc	ctatgagttt	540
ttcttagaat	gtataaaggt	tgtagcccat	cnaacttcaa	agaaaaaat	gaccacatac	600
tttgcaatca	ggctgaaatg	tgcatgctn	ttctaattcc	aactttataa	actagcaaan	660
aagtg						665

&lt;210&gt; 197

&lt;211&gt; 492

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(492)

<223> n = A,T,C or G

<400> 197

ttttnttttt	ttttttttgc	aggaaggatt	ccattttattg	tggatgcatt	ttcacaatat	60
atgtttattg	gagcgatcca	ttatcagtga	aaagtatcaa	gtgtttataa	natttttagg	120
aaggcagatt	cacagaacat	gctngtcngc	ttgcagtttt	acctcgtna	gatnacagag	180
aattatagtc	naaccagtaa	acnaggaatt	tacttttcaa	aagattaaat	ccaaactgaa	240
caaaattcta	ccctgaaact	tactccatcc	aaatattgga	ataanagtca	gcagtgatac	300
attctcttct	gaactttaga	ttttctagaa	aaatatgtaa	tagtgatcag	gaagagctct	360
tgttcaaaag	tacaacnaag	caatgttccc	ttaccatagg	ccttaattca	aactttgatc	420
catttcactc	ccatcacggg	agtcaatgct	acctgggaca	cttgtatttt	gttcatnctg	480
ancntggctt	aa					492

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(478)

<223> n = A,T,C or G

<400> 198

ttntttttgn	atttcantct	gtannaanta	ttttcattat	gtttattana	aaaatatnaa	60
tgtntccacn	acaaatcatn	ttacntnagt	aagaggccan	ctacattgta	caacatacac	120
tgagtatat	ttgaaaagga	caagtttaaa	gtanacncat	attgccganc	atancacatt	180
tatacatggc	ttgattgata	tttagcacag	canaaaactga	gtgagttacc	agaaanaaat	240
nataatgtc	aatcngattt	aagatacaaa	acagatccta	tggtacatan	catcntgtag	300
gagttgtggc	tttatgttta	ctgaaagtca	atgcagttcc	tgtacaaaag	gatggccgta	360
agcattctag	tacctctact	ccatgggtta	gaatcgtaca	cttatgttta	catatgtnc	420
gggtaagaat	tgtgttaagt	naanttattg	agaggtccan	gagaaaaatt	tgatncaa	478

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 199

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtcc	tgctcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttctcttac	ggatgagaga	ctggctcaag	aatatcctca	tgtagcttta	240
tgaagccnac	tctgaacacg	ctggttatct	nagatgagaa	ncagagaaat	aaagtcnaga	300
aaatttacct	ggangaaaag	aggcttngg	ctggggacca	tccattgaa	ccttctctta	360
anggacttta	agaanaaact	accacatgtn	tgtngtatcc	tggtgccngg	ccgtttantg	420
aacntngacn	ncacccttnt	ggaatanant	cttgacngcn	tcctgaactt	gctcctctgc	480
ga						482

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(270)  
 <223> n = A,T,C or G

<400> 200  
 cgcccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc 60  
 cgactgcgac gacggcgccg gcgacagtcg cagggtgcagc ggcggcgccct ggggtcttgc 120  
 aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga 180  
 cagccggaac agagcccggg gaangcggga ggcctcgggg agcccctcgg gaaggcgccg 240  
 ccgagagata cgcaggtgca ggtggccgcc 270

<210> 201  
 <211> 419  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(419)  
 <223> n = A,T,C or G

<400> 201  
 tttttttttt ttttggaaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca 60  
 gctagcaagg taacagggtta gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg 120  
 ttgattgggt tgtctttatg gggcgccggg ggggtagggg aaancgaagc anaantaaca 180  
 tggagtgggt gcacctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg 240  
 tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag 300  
 tccactgtnt ctggaggag attagggttt cttgccana tccaancaa atccacntga 360  
 aaaagtggga tgatncangt acngaatacc ganggcatan ttctcatant cggtgccca 419

<210> 202  
 <211> 509  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(509)  
 <223> n = A,T,C or G

<400> 202  
 tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
 tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng 120  
 gtnattttnc aaaatctaaa nnttatcaaa atntnagcca aantccttac ncaaatnnaa 180  
 tacnncnaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa 240  
 aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atnttttnnaa 300  
 ggaactaaaa taataaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta 360  
 caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng 420  
 ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480  
 caatggnaat ncnccnccnc tggactagt 509

<210> 203  
 <211> 583  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(583)  
 <223> n = A,T,C or G

<400> 203  
 tttttttttt ttttttttga cccccctctt ataaaaaaca agttaccatt ttattttact 60  
 tacacatatt ttttttataa ttggtatttag atattcaaaa ggcagctttt aaaatcaaac 120  
 taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt 180  
 gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240  
 atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt 300  
 gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttctaaa 360  
 agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca ttttctacc 420  
 tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg 480  
 tccatttttag tcaactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt 540  
 attcaaaagc taatataaga ttttccacat actcatcttt ctg 583

<210> 204  
 <211> 589  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(589)  
 <223> n = A,T,C or G

<400> 204  
 ttttttttnt tttttttttt ttttttntct ttcttttttt ttganaatga ggatcgagtt 60  
 tttcactctc tagatagggc atgaagaaaa ctcatctttc cagcttttaa ataacaatca 120  
 aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc 180  
 tgaaggaaa ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat 240  
 tgagaggttt ttcttctcta ttacacata ttttccatg tgaatttgta tcaaaccctt 300  
 attttcatgc aaactagaaa ataattgtnt cttttgcata agagaagaga acaatatnag 360  
 cattacaaa ctgctcaaat tgtttgtaa gnttatccat tataattagt tnggcaggag 420  
 ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaataatcc 480  
 aaaataatta aaggaacatt ttagccttg gtataattag ctaattcact ttacaagcat 540  
 ttattnagaa tgaattcaca tgttattatt cctagcccca acacaatgg 589

<210> 205  
 <211> 545  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(545)  
 <223> n = A,T,C or G

<400> 205  
 tttttntttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat 60  
 agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata 120  
 tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaatat 180  
 ttaagatcat agagcttgta agtgaagaaga taaaatttga cctcagaac tctgagcatt 240  
 aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat 300  
 atgggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct 360  
 tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt 420  
 aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatng 480

aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga 540  
aacco 545

<210> 206  
<211> 487  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(487)  
<223> n = A,T,C or G

<400> 206  
tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt 60  
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna 120  
caatttataa atgtaagggt ccattattga gtanatatat tcctccaaga gtggatgtgt 180  
cccttctccc accaactaat gaancagcaa cattagttaa attttattag tagatnatac 240  
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag 300  
ttggttagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt 360  
tcggtagaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cggtaggcaag 420  
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt 480  
ttcaaaa 487

<210> 207  
<211> 332  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(332)  
<223> n = A,T,C or G

<400> 207  
tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa 60  
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact 120  
gcatttatag gaccttctgg tgggtctgct gttacntttg aantctgaca atccttgana 180  
atcctttgcat gcagaggagg taaaaggat tggattttca cagaggaana acacagcgca 240  
gaaatgaagg gccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg 300  
aaaagaaggc agcctaggcc ctggggagcc ca 332

<210> 208  
<211> 524  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(524)  
<223> n = A,T,C or G

<400> 208  
agggcgtggt gcggaggcgt ttactgtttt gtctcagtaa caataaatat aaaaagactg 60  
gttgtgttcc ggcccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat 120  
tttaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac 180  
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtcatact tgtaataact 240  
tttggcagaa tacttnttga aacttgcala tgataactaa gatccaagat atttcccaaa 300



gtaaatagaa	gtgggtcata	atattaatta	cctgttcaca	tcagcttcca	tttacaagtc	360
atgagcccag	acactgacat	caaactaagc	ccacttagac	tcctcaccac	cagtctgtcc	420
tgatcatcaga	caggaggctg	tcaccttgac	caaattctca	ccagtcaatc	atctatccaa	480
aaaccattac	ctgatccact	tccggtaatg	caccaccttg	gtga		524

&lt;210&gt; 209

&lt;211&gt; 159

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 209

gggtgaggaa	atccagagtt	gccatggaga	aaattccagt	gtcagcattc	ttgctccttg	60
tgccctctc	ctacactctg	gccagagata	ccacagtcaa	acctggagcc	aaaaaggaca	120
caaaggactc	tcgacccaaa	ctgcccaga	ccctctcca			159

&lt;210&gt; 210

&lt;211&gt; 256

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(256)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 210

actccctggc	agacaaaggc	agaggagaga	gctctgttag	ttctgtgttg	ttgaactgcc	60
actgaatttc	tttccacttg	gactattaca	tgccanttga	gggactaatg	gaaaaacgta	120
tgaggagatt	ttanccaatt	tangtntgta	aatggggaga	ctggggcagg	cgggagagat	180
ttgcagggtg	naaatgggan	ggctggtttg	ttanatgaac	agggacatag	gaggtaggca	240
ccaggatgct	aatca					256

&lt;210&gt; 211

&lt;211&gt; 264

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(264)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 211

acattgtttt	tttgagataa	agcattgaga	gagctctcct	taacgtgaca	caatggaagg	60
actggaacac	ataccacat	ctttgttctg	agggataatt	ttctgataaa	gtcttgtctg	120
atattcaagc	acatatgtta	tatattattc	agttccatgt	ttatagccta	gttaaggaga	180
ggggagatac	attcngaaag	aggactgaaa	gaaatactca	agtnngaaaa	cagaaaaaga	240
aaaaaaggag	caaatgagaa	gcct				264

&lt;210&gt; 212

&lt;211&gt; 328

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(328)

&lt;223&gt; n = A,T,C or G

<400> 212  
 acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa 60  
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120  
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccggcag 180  
 ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta 240  
 cccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca 300  
 ttttttttct ctttattcct ttgtcaga 328

<210> 213  
 <211> 250  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(250)  
 <223> n = A,T,C or G

<400> 213  
 acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt 60  
 taaagcattg ctcaactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120  
 cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt 180  
 ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct 240  
 tctcatcggt 250

<210> 214  
 <211> 444  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(444)  
 <223> n = A,T,C or G

<400> 214  
 acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag 60  
 gatttaatgt tgtctcagct ttgggcacttc agttaggacc taaggatgcc agccggcag 120  
 tttatatatg cagcaacaat attcaagcgc gacaacaggc tattgaactt gcccggcag 180  
 tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac 240  
 ccctacgact ctttactctc tggagagggc cagtgggtgg agctataagc ttggccacat 300  
 ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag 360  
 agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt 420  
 actttgctct ccctaataata cctc 444

<210> 215  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(366)  
 <223> n = A,T,C or G

<400> 215  
 acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt 60

taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgcc	aagganatat	acatttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcataaacct	gctgataagc	catgttgaga	aacaaatata	tctctgacct	240
tctcatcggt	aagcagaggc	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	ttctacact	gtaaccaggt	ttccaaccaa	ggtggaaatc	tcctatactt	360
ggtgcc						366

<210> 216  
 <211> 260  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(260)  
 <223> n = A,T,C or G

ctgtataaac	agaactccac	tgcanagagg	agggccgggc	caggagaatc	tccgcttgtc	60
caagacaggg	gcctaaggag	ggtctccaca	ctgctnntaa	gggctnttnc	atttttttat	120
taataaaaag	tnnaaaaggc	ctcttctcaa	cttttttccc	ttnggctgga	aaatttaaaa	180
atcaaaaatt	tcctnaagtt	ntcaagctat	catatatact	ntatcctgaa	aaagcaacat	240
aatttctcct	tcctcctttt					260

<210> 217  
 <211> 262  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

acctacgtgg	gtaagtttan	aaatgttata	atttcaggaa	naggaacgca	tataattgta	60
tcttgccctat	aattttctat	tttaataagg	aaatagcaaa	ttgggggtggg	gggaatgtag	120
ggcattctac	agtgttgagca	aaatgcaatt	aaatgtggaa	ggacagcact	gaaaaatttt	180
atgaataatc	tgtatgatta	tatgtctcta	gagtagattt	ataattagcc	acttacccta	240
atatacctca	tgcttgtaaa	gt				262

<210> 218  
 <211> 205  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(205)  
 <223> n = A,T,C or G

accaaggtgg	tgcatcaccg	gaantggatc	aangacacca	tcgtggccaa	cccctgagca	60
cccctatcaa	ctcccctttg	tagtaaaactt	ggaaccttgg	aaatgaccag	gccaagactc	120
aggcctcccc	agttctactg	acctttgtcc	ttangtnna	ngtccagggt	tgctaggaaa	180
anaaatcagc	agacacaggt	gtaaa				205

<210> 219

<211> 114  
 <212> DNA  
 <213> Homo sapien

<400> 219  
 tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gccccatcca 60  
 accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
 <211> 93  
 <212> DNA  
 <213> Homo sapien

<400> 220  
 actagccagc acaaaaggca gggtagcctg aattgctttt tgctctttac atttctttta 60  
 aaataagcat ttagtgctca gtccctactg agt 93

<210> 221  
 <211> 167  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(167)  
 <223> n = A,T,C or G

<400> 221  
 actangtgca ggtgcgcaca aatatttgct gatattccct tcatcttgga ttccatgagg 60  
 tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc 120  
 cccccactac cttccctgac gctcccccana aatcacccaa cctctgt 167

<210> 222  
 <211> 351  
 <212> DNA  
 <213> Homo sapien

<400> 222  
 agggcgtggt gcgaggggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60  
 gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa 120  
 atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180  
 ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240  
 taggtgagca tgattagaga gctttaggtg tgcttttaca tatactctggc atatttgagt 300  
 ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(383)  
 <223> n = A,T,C or G

<400> 223  
 aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60  
 tggtaattat ggtcaattta atwrtttkt ggggcatttc cttacattgt cttgacaaga 120

ttaaaatgtc	tgtgccaaaa	ttttgtat	tatttgaga	cttcttatca	aaagtaatgc	180
tgccaaagga	agtctaagga	attagtagtg	ttcccmcac	ttgtttggag	tgtgctattc	240
taaaagattt	tgatttcctg	gaatgacaat	tatatattta	ctttggtggg	ggaaanagtt	300
ataggaccac	agtcttcact	tctgatactt	gtaaattaat	cttttattgc	acttgttttg	360
accattaagc	tatatgttta	aaa				383

<210> 224  
 <211> 320  
 <212> DNA  
 <213> Homo sapien

ccccgaagg	cttcttgta	gaaaatagta	cagttacaac	caataggaac	aacaaaaaga	60
aaaagtttgt	gacattgtag	tagggagtgt	gtaccctta	ctcccatca	aaaaaaaaat	120
ggatacatgg	ttaaaggata	raagggaat	attttatcat	atgttctaaa	agagaaggaa	180
gagaaaatac	tactttctcr	aaatggaagc	ccttaaagggt	gctttgatac	tgaaggacac	240
aaatgtggcc	gtccatcctc	ctttaragtt	gcagtacttg	gacacggtaa	ctgttgagtt	300
tttaractcm	gcattgtgac					320

<210> 225  
 <211> 1214  
 <212> DNA  
 <213> Homo sapien

gaggactgca	gcccgcactc	gcagccctgg	caggcgccac	tggatcatga	aaacgaattg	60
ttctgctcgg	gcgtcctggg	gcacccgcag	tgggtgctgt	cagccgcaca	ctgtttccag	120
aactcctaca	ccatcgggct	gggcctgcac	agtcttgagg	ccgaccaaga	gccaggggagc	180
cagatggtgg	aggccagcct	ctccgtacgg	cacccagagt	acaacagacc	cttgctcgct	240
aacgacctca	tgctcatcaa	gttgacgaa	tccgtgtccg	agtctgacac	catccggagc	300
atcagcattg	cttcgcagtg	ccctaccgag	gggaactctt	gcctcggttc	tggctggggg	360
ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	tgaacgtgtc	gggtggtgtct	420
gaggaggctc	gcagtaagct	ctatgaccgg	ctgtaccacc	ccagcatggt	ctgcgccggc	480
ggaggggcaag	accagaagga	ctcctgcaac	ggtgactctg	ggggggccct	gatctgcaac	540
gggtacttgc	agggccttgt	gtctttcgga	aaagcccgtg	gtggccaagt	tggcgtgccca	600
ggtgtctaca	ccaacctctg	caaattcact	gagtgatag	agaaaaccgt	ccaggccagt	660
taactctggg	gactgggaac	ccatgaatt	gacccccaaa	tacatcctgc	ggaaggaatt	720
caggaatatc	tggtcccagc	ccctcctccc	tcaggccag	gagtcagggc	ccccagcccc	780
tcctccctca	aaaccaagggt	acagatcccc	agcccctcct	ccctcagacc	caggagtcca	840
gacccccag	cccctcctcc	ctcagaccca	ggagtccagc	ccctcctccc	tcagaccag	900
gagtcagac	ccccagcccc	ctcctccctc	agaccagggg	gtccaggccc	ccaaccctc	960
ctccctcaga	ctcagaggtc	caagccccc	acccctcctt	ccccagacc	agaggtccag	1020
gtcccagccc	ctcctccctc	agaccagcg	gtccaatgcc	acctagactc	tccctgtaca	1080
cagtgccccc	ttgtggcag	ttgacccaac	cttaccagtt	ggtttttcat	ttttgtccc	1140
tttcccctag	atccagaaat	aaagtctaag	agaagcgcaa	aaaaaaaaaa	aaaaaaaaaa	1200
aaaaaaaaaa	aaaa					1214

<210> 226  
 <211> 119  
 <212> DNA  
 <213> Homo sapien

accagtatg	tgacgggaga	cggaacccca	tgtgacagcc	cactccacca	gggttcccaa	60
agaacctggc	ccagtcataa	tcattcatcc	tgacagtggc	aataatcacg	ataaccagt	119

<210> 227  
 <211> 818

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 227

acaattcata	gggacgacca	atgaggacag	ggaatgaacc	cggtctctcc	ccagccctga	60
tttttgctac	atatggggtc	ccttttcatt	ctttgcaaaa	acactgggtt	ttctgagaac	120
acggacgggt	cttagcacaa	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttctct	ctctggagga	aaggtggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgtcccc	ttccaatcag	ccacttctga	gaacccccat	ctaacttcct	actggaaaag	360
agggcctcct	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420
ggaaagggty	caccctcagc	agagaagccg	agagcttaac	tctggtcggt	tccagagaca	480
acctgctggc	tgtcttgga	tgcgccagc	ctttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcatgagagg	600
gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggtc	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	aggttttcag	cctagatggg	agtcgtgt			818

&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggtctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaacga	gcctcctcct	tggaagatgg	aagaccgtgt	120
tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggctctgtaa	aatagaagag	cagtcaactgt	ggaactacca	aatggcgaga	240
tgctcgggtc	acattggggg	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtc	acctctgcag	360
gctggcagct	gaatggcttg	ccgggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacggty	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctgggtga	cagtgaaccg	540
ccgtgggtatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttggggtttg	600
ttcttttctg	taatgttctc	ctgtgttgtc	agctgtcttc	atttcctggg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttcactctg	aagtagctgg	tggt				744

&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcatgtgaac	60
cattacacat	cgaataaaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgacagggtg	ttgtttttta	attattattg	ttagaaacgt	caccacacgt	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagctc	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

cagcagaaca	aatacaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
------------	-----------	------------	------------	------------	------------	----

gagcgacagt tcaaggagga gaagcttgca gagcagctca agcaagctga ggagctcagg 120  
 caatataaag tcctgggtca cactcaggaa cgagagctga ccaggttaag ggagaagttg 180  
 cgggaaggga gagatgcctc cctctcattg aatgagcatc tccaggccct cctcactccg 240  
 gatgaaccgg acaagtccca ggggcaggac ctccaagaaa cagacctcgg ccgcgaccac 300  
 g 301

<210> 231  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 231  
 gcaagcacgc tggcaaactc ctgtcaggtc agctccagag aagccattag tcatttttagc 60  
 caggaactcc aagtccacat ccttggcaac tggggacttg cgcagggttag ccttgaggat 120  
 ggcaacacgg gactttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180  
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240  
 tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300  
 c 301

<210> 232  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 232  
 agtaggtatt tcgtgagaag ttcaacacca aaactggaac atagtctctcc ttcaagtgtt 60  
 ggcgacagcg gggcttcctg attctggaat ataactttgt gtaaattaac agccacctat 120  
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca 180  
 cgtgctgtac caagtgtcgg tgccagcctg ttacctgttc tctactgaaa tctgggcta 240  
 gctcttctgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300  
 g 301

<210> 233  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 233  
 atgactgact tcccagtaag gctctctaag gggtaagtag gaggatccac aggatttgag 60  
 atgctaaggc ccagagatc gtttgatcca accctcttat ttccagaggg gaaaatggg 120  
 cctagaagtt acagagcatc tagctggtgc gctggcacc cttggcctcac acagactccc 180  
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240  
 taaaaattaa catgagatga gttagagactt tattgagaaa gcaagagaaa atcctatcaa 300  
 c 301

<210> 234  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 234  
 aggtcctaca catcgagact catccatgat tgatataaat ttaaaaatta caagcaaaga 60  
 cattttattc atcatgatgc tttcttttct ttcttctttt cgttttcttc tttttctttt 120  
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180  
 cgcctcatga cagcaagtgc aatgtttttg ccacctgact gaaccacttc caggagtgc 240  
 ttgatcacca gcttaatggt cagatcatct gcttcaatgg ctctgtcagt atagtctctc 300  
 t 301

<210> 235  
 <211> 283  
 <212> DNA  
 <213> Homo sapien

<400> 235  
 tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg 60  
 aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg 120  
 tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata 180  
 atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatcaaca 240  
 ttagggattc aaagaaatat tagatttaag ctcacactgg tca 283

<210> 236  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 236  
 aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata 60  
 aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg 120  
 tcggagcagc atcathtaata ccaagcagaa tgcgtaatag ataaatacaa tggatatag 180  
 tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta 240  
 aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc 300  
 a 301

<210> 237  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 237  
 cagtggtagt ggtggtggac gtggcgttgg tcgtggtgcc ttttttggtg cccgtcacaa 60  
 actcaatttt tgttcgctcc tttttggcct ttccaattt gtccatctca attttctggg 120  
 ccttggtctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacataatcct 180  
 ttgggtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta 240  
 gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctcctttatc 300  
 t 301

<210> 238  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 238  
 gggcaggttt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgaact 60  
 gttcacagtt cagcccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca 120  
 ccttgagact tccggagtcg aggctctcca gggttcccca gcccatcaat cattttctgc 180  
 acccctgccc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca 240  
 gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta 300  
 t 301

<210> 239  
 <211> 239  
 <212> DNA  
 <213> Homo sapien

<400> 239  
 ataagcagct aggggaattct ttatttagta atgtcctaac ataaaagttc acataactgc 60



ttctgtcaaa	ccatgatact	gagctttgtg	acaaccaga	aataactaag	agaaggcaaa	120
cataatacct	tagagatcaa	gaaacattta	cacagttcaa	ctgtttaaaa	atagctcaac	180
attcagccag	tgagtagagt	gtgaatgcca	gcatacacag	tatacaggtc	cttcaggga	239

<210> 240  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 240						
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gggatctgcc	ctccagtgga	accttttaag	gaagaagtgg	gccaagcta	agttccacat	120
gctgggtgag	ccagatgact	tctgttcctt	ggtcactttc	ttcaatgggg	cgaatggggg	180
ctgccagggt	tttaaaatca	tgcttcatct	tgaagcacac	ggtcacttca	ccctcctcac	240
gctgtgggtg	tactttgatg	aaaataccca	ctttgttggc	ctttctgaag	ctataatgtc	300

<210> 241  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 241						
gagggtctggt	gctgaggtct	ctgggctagg	aagaggagtt	ctgtggagct	ggaagccaga	60
cctctttgga	ggaaactcca	gcagctatgt	tgggtgtctct	gagggaatgc	aacaaggctg	120
ctcctccatg	tattggaaaa	ctgcaaaactg	gactcaactg	gaaggaagtg	ctgctgccag	180
tgtgaagaac	cagcctgagg	tgacagaaac	ggaagcaaac	aggaacagcc	agtcttttct	240
tcctcctcct	gtcatagcgt	ctctctcaag	catcctttgt	tgtcaggggc	ctaaaaggga	300
g						301

<210> 242  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 242						
cagaggtcct	gggatgcaac	caatcactct	gtttcacgtg	acttttatca	ccatacaatt	60
tgtggcattt	cctcattttc	tacattgtag	aatcaagagt	gtaaataaat	gtatatcgat	120
gtcttcaaga	atatatcatt	cctttttcac	tagaaccat	tcaaatata	agtcaagaat	180
cttaatatca	acaaatatat	caagcaaact	ggaaggcaga	ataactacca	taatttagta	240
taagtaacca	aagttttata	aatcaaaagc	cctaattgata	accattttta	gaattcaatc	300
a						301

<210> 243  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 243						
aggtaagtcc	cagtttgaag	ctcaaaagat	ctggtatgag	cataggctca	tcgacgacat	60
ggtggcccaa	gctatgaaat	cagagggagg	cttcactctg	gcctgtaaaa	actatgatgg	120
tgacgtgcag	tcggactctg	tgcccaagg	gtatggctct	ctcggcatga	tgaccagcgt	180
gctggtttgt	ccagatggca	agacagtaga	agcagaggct	gccacggga	ctgtaaccgg	240
tcactaccgc	atgttccaga	aaggacagga	gacgtccacc	aatcccattg	cttccatttt	300
t						301

<210> 244  
 <211> 300  
 <212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 244

gctggtttgc	aagaatgaaa	tgaatgattc	tacagctagg	acttaacctt	gaaatggaaa	60
gtcatgcaat	cccatttgca	ggatctgtct	gtgcacatgc	ctctgtagag	agcagcattc	120
ccagggacct	tggaacagct	tgacactgta	aggtgcttgc	tccccaagac	acatcctaaa	180
aggtgttgta	atggtgaaaa	cgtcttcctt	ctttattgcc	ccttcttatt	tatgtgaaca	240
actgtttgtc	ttttgtgtat	cttttttaaa	ctgtaaagtt	caattgtgaa	aatgaatatc	300

&lt;210&gt; 245

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 245

gtctgagtat	ttaaaatggt	attgaaatta	tccccaacca	atgttagaaa	agaaagaggt	60
tatatactta	gataaaaaat	gaggtgaatt	actatccatt	gaaatcatgc	tcttagaatt	120
aaggccagga	gatattgtca	ttaatgtara	cttcaggaca	ctagagtata	gcagccctat	180
gttttcaaag	agcagagatg	caattaaata	ttgttttagca	tcaaaaaggc	cactcaatac	240
agctaataaa	atgaaagacc	taatttctaa	agcaattctt	tataatttac	aaagttttaa	300
g						301

&lt;210&gt; 246

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 246

ggtctgtcct	acaatgcctg	cttcttgaaa	gaagtcggca	ctttctagaa	tagctaaata	60
acctgggctt	attttaaaga	actatttgta	gctcagattg	gttttctat	ggctaaaata	120
agtgcctctt	gtgaaaatta	aataaaacag	ttaattcaaa	gccttgatat	atgttaccac	180
taacaatcat	actaaatata	ttttgaagta	caaagtttga	catgctctaa	agtgacaacc	240
caaatgtgtc	ttacaaaaca	cgttcctaac	aaggatgctt	ttacactacc	aatgcagaaa	300
c						301

&lt;210&gt; 247

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 247

aggtcctttg	gcagggtctca	tggatcagag	ctcaaaactgg	agggaaaggc	atttcgggta	60
gcctaagagg	gcgactggcg	gcagcacaac	caaggaaggc	aaggttgttt	ccccacgct	120
gtgtcctgtg	ttcaggtgcg	acacacaatc	ctcatgggaa	caggatcacc	catgcgctgc	180
ccttgatgat	caaggttggg	gcttaagtgg	attaaggag	gcaagttctg	ggttccttgc	240
cttttcaaac	catgaagtca	ggctctgtat	ccctcctttt	cctaactgat	attctaacta	300
a						301

&lt;210&gt; 248

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 248

aggtccttgg	agatgccatt	tcagccgaag	gactcttctw	ttcggaagta	caccctcact	60
attaggaaga	ttcttagggg	taatttttct	gaggaaggag	aactagccaa	cttaagaatt	120
acaggaagaa	agtggtttgg	aagacagcca	aagaaataaa	agcagattaa	attgtatcag	180
gtacattcca	gcctgttggc	aactccataa	aaacatttca	gattttaatc	ccgaatttag	240

ctaattgagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc 300  
c 301

<210> 249  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 249  
gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag 60  
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgcc 120  
ccagggagac acagcagtga ctcagagctg gtgcgacact gtgcctccct cctcaccgcc 180  
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag 240  
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt 300  
a 301

<210> 250  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 250  
ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc 60  
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc 120  
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac 180  
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta 240  
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc 300  
a 301

<210> 251  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 251  
gccgaggtcc tacatttggc ccagtttccc cctgcacccct ctccagggcc cctgcctcat 60  
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat 120  
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct 180  
cattgggata aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgaa 240  
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct 300  
c 301

<210> 252  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 252  
gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttctca 60  
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata 120  
tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa 180  
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaagt 240  
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc 300  
a 301

<210> 253  
<211> 301  
<212> DNA

<213> Homo sapien

<400> 253

ttccctaaga	agatgttatt	ttgttgggtt	ttgttcccc	tccatctcga	ttctcgtacc	60
caactaaaa	aaaaaataa	agaaaaaatg	tgctgcgttc	tgaaaaataa	ctccttagct	120
tggtctgatt	gttttcagac	cttaaaatat	aaacttggtt	cacaagcttt	aatccatgtg	180
gatttttttt	cttagagaac	cacaaaacat	aaaaggagca	agtcggactg	aatacctgtt	240
tccatagtgc	ccacagggtg	ttcctcacat	tttctccata	ggaaaatgct	ttttcccaag	300
g						301

<210> 254

<211> 301

<212> DNA

<213> Homo sapien

<400> 254

cgctgcgcct	ttcccttggg	ggaggggcaa	ggccagaggg	ggtccaagtg	cagcacgagg	60
aacttgacca	attcccttga	agcgggtggg	ttaaaccctg	taaatgggaa	caaaatcccc	120
ccaaatctct	tcattcttacc	ctggtggact	cctgactgta	gaattttttg	gttgaaacaa	180
gaaaaaata	aagcttttga	cttttcaagg	ttgcttaaca	ggtactgaaa	gactggcctc	240
acttaaaactg	agccaggaaa	agctgcagat	ttattaatgg	gtgtgttagt	gtgcagtgcc	300
t						301

<210> 255

<211> 302

<212> DNA

<213> Homo sapien

<400> 255

agcttttttt	tttttttttt	tttttttttt	ttcattaaaa	aatagtgtct	tttattataa	60
attactgaaa	tgtttctttt	ctgaatataa	atataaatat	gtgcaaagtt	tgacttggat	120
tggtgatttg	ttgagttctt	caagcatctc	ctaataccct	caagggcctg	agtagggggg	180
aggaaaaagg	actggaggtg	gaatctttat	aaaaaacaag	agtgattgag	gcagattgta	240
aacattatta	aaaaacaaga	aacaacaaaa	aaaatagaga	aaaaaacac	cccaacacac	300
aa						302

<210> 256

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 256

gttccagaaa	acattgaagg	tggtttccca	aagtctaact	agggataccc	cctctagcct	60
aggaccctcc	tccccacacc	tcaatccacc	aaaccatcca	taatgcaccc	agataggccc	120
acccccaaaa	gcctggacac	cttgagcaca	cagttatgac	caggacagac	tcattcttat	180
aggcaaatag	ctgctggcaa	actggcatta	cctggtttgt	ggggatgggg	gggcaagtgt	240
gtggcctctc	ggcctgggta	gcaagaacat	tcagggtagg	cctaagttan	tcgtgttagt	300
t						301

<210> 257

<211> 301

<212> DNA

<213> Homo sapien

&lt;400&gt; 257

gttgtggagg aactctggct tgctcattaa gtcctactga ttttactat cccctgaatt	60
tccccactta tttttgtctt tcaactatcgc aggccttaga agaggtctac ctgcctccag	120
tottacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat	180
gtcacattac tcccttcagt gatttcttgt agaagtgcc atccctgaat gccaccaaga	240
tottaatctt cacatcttta atcttatctc tttgactcct ctttacacog gagaaggctc	300
c	301

&lt;210&gt; 258

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 258

cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc	60
aggggccgag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc	120
cccaggcaca caagaatcca ataccaggac tgggcaaaat cttcaaagat ctttaacactg	180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat	240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac	300
t	301

&lt;210&gt; 259

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 259

tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg	60
gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa	120
gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggtctgt	180
tccagctcac atctcatctg catgcagcac ggaccggatg cgcccactgg gtcttggctt	240
ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccagggtg	300
c	301

&lt;210&gt; 260

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 260

tttttttctt ccctaaggaa aaagaaggaa caagtctcat aaaaccaa atagcaatgg	60
aaggtgtctt aacttgaaaa agattaggag tcaactggtt acaagttata attgaatgaa	120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacaa caggattaac	180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc	240
actgagacat cagtacctgc ccggcgggcc gctcgagccc aattctgcag atatccatca	300
c	301

87

<210> 261  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 261  
 aaatattcga gcaaatacctg taactaatgt gtctccataa aaggctttga actcagtga 60  
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggtt 120  
 agcaccaact attccatata attcatcagc aggaataaaa ggctcttcag aagggttcaat 180  
 ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240  
 ggcagtgtga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300  
 a 301

<210> 262  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 262  
 gaggagagcc tggtacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60  
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc 120  
 cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga 180  
 gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgcgc 240  
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300  
 c 301

<210> 263  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 263  
 tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60  
 aaaatttacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg 120  
 ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat 180  
 taatgactga cttcccagta aggcctctta aggggtaagt angaggatcc acaggatttg 240  
 agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 300  
 g 301

<210> 264  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 264  
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60  
 aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag 120  
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180  
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240  
 acccttcata taaattcact atcttggctt gaggcactcc ataaaatgta tcacgtgcat 300  
 a 301

<210> 265

<211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 265  
 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactaactg tcattcttgt 60  
 cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 120  
 catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga 180  
 ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaa gaatccaaag 240  
 cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300  
 c 301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266  
 taccgtctgc ctttctctcc atccaggcca tctgcgaatc tacatgggtc ctctattcg 60  
 acaccagatc actctttcct ctaccacag gcttgctatg agcaagagac acaacctcct 120  
 ctcttctgtg ttccagcttc ttttctgtt cttccaccc cttaagttct attcctgggg 180  
 atagagacac caatacccat aacctctctc ctaagcctcc ttataacca ggggtgcacag 240  
 cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgcctg 300  
 a 301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267  
 aaagagcaca ggccagctca gcctgccttg gccatctaga ctcagccttg ctccatgggg 60  
 gttctcagtg ctgagtcctt ccaggaaaag ctcacctaga cttctgagg ctgaatcttc 120  
 atcctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtc ggagtaaagc 180  
 ctcatctga ttcctctcct tcttttctt caagttggct ttctcacaat ccctctgttc 240  
 aattcgcttc agcttgtctg ctttagccct catttcaga agcttcttct ctttggcatc 300  
 t 301

<210> 268  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 268  
 aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta 60  
 gatcttggga gagctgggtc ttctaaggag aaggaggag gacagatgta actttggatc 120  
 tcgaagagga agtctaattg aagtaattag tcaacggtcc ttgttttagac tcttggaata 180  
 tgctgggtgg ctcagtgagc ctttttgag aaagcaagta ttattcttaa ggagtaacca 240  
 cttccattg ttctactttc taccatcacc aattgtatat tatgtattct ttggagaact 300  
 a 301

<210> 269  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 269  
 taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat 60

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aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact 120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta 180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta 240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc 300
t 301

```

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<210> 270
<211> 301
<212> DNA
<213> Homo sapien

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<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgcct ataaaattaa ttaagcctta 60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120
gagcttgctg gtgcagtgc tattggataa cactattcat gccgaattg atcaagtcaa 180
ccaactcctt gaactggatc atcagaagaa ggggtgtgca cgatatactg cactagataa 240
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcct aacagaaaac 300
a 301

```

```

<210> 271
<211> 301
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

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<400> 271
aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt 60
tttatagctc atcttttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca 120
gaattgcaat cacttcatca gcctgtattc gtcceaattc tctataaagt gggccaagg 180
tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240
tctctcctcc agatganaac tgatcatgag cccacatttt gggttttata gaagcagtca 300
c 301

```

```

<210> 272
<211> 301
<212> DNA
<213> Homo sapien

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```

<400> 272
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaatgtc 60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcattccaca 180
gcatcttctc caacaaatat aaccttgagt ggcttcttgc aatctatgtt ctttgttttc 240
ctaaggactt ccattgcac tcctacaata ttttctctac gcaccactag aattaagcag 300
g 301

```

```

<210> 273
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)

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<223> n = A,T,C or G

<400> 273

acatgtgtgt atgtgtatct ttgggaaan aanaagacat cttgtttayt atttttttgg	60
agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa	120
gaaccgtcta aaaataaaat ttacatgtgc dtatattcct tatagtatgc ttatttcacc	180
tttcttctgt ccagagagag tatcagtgc ananattma ggggaamac atgmattgg	240
gggacttnty tttacngagm accctgccg sgcgccctcg makngantt ccgcsananc	300
t	301

<210> 274

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 274

cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg	60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa	120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca	180
tctaggtatg gttgcattct cgtctcttt tctgcagtag ataatgaggt aaccgaaggc	240
aattgtgctt cttttgataa gaagctttct tggcatatc aggaaattcc aganaaagtc	300
c	301

<210> 275

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 275

tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg	60
gggtgaaatt ggccaacttt ctattaactt atgttggtcaa ttttgccacc aacagtaagc	120
tgcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtgag	180
tcaagagact ccaggcctc agcgtacctg ccggggcggc cgctcgaagc cgaattctgc	240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat	300
a	301

<210> 276

<211> 301

<212> DNA

<213> Homo sapien

<400> 276

tgtacacata ctcaataaat aaatgactgc attgtggat tattactata ctgattatat	60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat	120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc	180
caatacattht aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt	240
aaaactattht agtatgtttht ccttgcttca tgtctgagaa ggctctcctt caatggggat	300
g	301

<210> 277  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccca ccctcgtcct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttnctgtgc gattacatct gaccagtctc cttttccga agtcntccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca 120  
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180  
 aatgaacatc tcagtgtgac tcacaatggt ctggcactat tataagtgtc tcacaggttt 240  
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt accttccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 280

ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg	60
tagaaagggtg gtggaaccaa attgtgggtca atggaaatag gagaatatgg ttctcactct	120
tgagaaaaaa acctaagatt agcccaggta gtgacctgta acttcagttt ttctgcctgg	180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga	240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag	300
t	301

&lt;210&gt; 281

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 281

aggtaacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc	60
gccgagcaat ccaaatcctg aatgaagggg catcttctga aaaaggagat ctgaatctca	120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa	180
tgtgtagcac actgcgatta cagctaaata acccgatttt gtgtgtcatg tttgcatttc	240
tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagt gcatgacctc	300
g	301

&lt;210&gt; 282

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 282

caggctactac agaattaataa tactgacaag caagtagttt cttggcgtgc acgaattgca	60
tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctgacacaga	120
agcgcagaag caaagcccag gcagaacat gctaacctta cagctcagcc tgcacagaag	180
cgagaagca aagcccagc agaaccatgc taaccttaca gctcagcctg cacagaagcg	240
cagaagcaaa gccaggcgag aacatgctaa ccttacagct cagcctgcac agaagcacag	300
a	301

&lt;210&gt; 283

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 283

atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag	60
cacttttagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca	120
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc	180
acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcatctttta	240
ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt	300
g	301

&lt;210&gt; 284

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 284

caggtaaaaa acgctattaa gtggcttaga atttgaacat ttgtggtctt tatttacttt	60
gcttcgtgtg tgggcaaagc aacatcttcc cttaaataat attaccaaga aaagcaagaa	120
gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcat	180

ggtgagaggc aaggcatgag agggcaagtt tgttggtggac agatctgtgc ctactttatt	240
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt	300
a	301

<210> 285  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (301)  
 <223> n = A,T,C or G

<400> 285	
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc	60
aatgatcatt agtggttttaa aaaaaataact gaaaactcct tctgcatccc aatctctaac	120
caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg	180
attaaatatg tctgacttct tttgaggtca cagcactagg caaatgctat ttacgatctg	240
caaaagctgt ttgaagagtc aaagcccca tgtgaacagc atttctggac cctgtaacag	300
t	301

<210> 286  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 286	
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct	60
tgtatatattat ttttgcccta cagtggatca ttctagtagg aaaggacagt aagatttttt	120
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca	180
aaaataagct accatatagc ttataagctc caaatttttg ccttttacta aaatgtgatt	240
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt tttcccttg	300
t	301

<210> 287  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 287	
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg	60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg	120
aaatgatttg gttatgaacg cacagttagg gcagcagggc cagaatcctg accctctgcc	180
ccgtggttat ctctcccca gcttggtgc ctcatgttat cacagtattc cattttgttt	240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt ttcctctca ttggtaatgc	300
t	301

<210> 288  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 288	
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag	60
agtcaatagg aagacaaatt ccagttccag ctcatctggg gtatctgcaa agctgcaaaa	120
gatctttaaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatat	180
aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag	240

tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
a 301

<210> 289

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 289

ggtacactgt ttccatgta tgtttctaca cattgctacc tcagtgtcc tggaaactta 60  
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120  
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180  
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga 240  
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga 300  
a 301

<210> 290

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 290

acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60  
tgactgatct gttcatttct ctacagctc ttaccccaa aagcttttcc accctaagtg 120  
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg 180  
gagttctatc aagaggcaga aacagcacag aatccagtt ttaccattcg ctacagtgac 240  
tgccctgaac aaaaacattt ctccatgtct ctttttcttc atgcctcaag taacagtga 300  
a 301

<210> 291

<211> 301

<212> DNA

<213> Homo sapien

<400> 291

caggtaccaa tttcttctat cctagaacaa ttccatttta tgttgttgaa acataacaac 60  
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120  
tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat 180  
agccatggct gtttacttca tttaatattt ttagcataaa gacattatga aaaggcctaa 240  
acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct 300  
a 301

<210> 292

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 292  
 accttttagt agtaattgtct aataataaat aagaaatcaa ttttataagg tccatatagc 60  
 tgtattaaat aatttttaag tttaaaagat aaaataccat catttttaaat gttggtattc 120  
 aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg 180  
 ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc 240  
 tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa 300  
 a 301

<210> 293  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 293  
 ggtaccaagt gctggtgcc aacctgttacc tgttctcact gaaaagtctg gctaattgctc 60  
 ttgtgtagtgc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt 120  
 aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt 180  
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg 240  
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat 300  
 g 301

<210> 294  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 294  
 tgacccataa caatatacac tagctatctt ttttaactgtc catcattagc accaatgaag 60  
 attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag 120  
 ttttaactata gtcacaganc ttaaattatc acattgtttt ctatgtctac tgaaaataag 180  
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc 240  
 cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt 300  
 t 301

<210> 295  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 295  
 gtactctttc tctccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta 60  
 cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggtagaa aaactrtctga agagctagtc tatcagcatc tgacaggtag attggatggg 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataat tagtttgggt 300  
 tctct 305

<210> 296  
 <211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 296

aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct	60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg	120
attaaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac	180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt	240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg	300
c	301

&lt;210&gt; 297

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(300)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 297

actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta	60
aagggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga	120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt	180
tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc	240
accgcacctc ggcgcgcgacc acgctaagcc gaattctgca gatatccatc aactggcgg	300

&lt;210&gt; 298

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 298

tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg	60
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg	120
tgaagctctc agatcaatca cgggaagggc ctggcggtgg tggccacctg gaaccaccct	180
gtcctgtctg tttacatttc actaycaggt tttctctggg cattacnatt tgttccccta	240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcagggtggct ctcagcgagg	300
t	301

&lt;210&gt; 299

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 299

gttttgagac ggagtttcac tcttggtgcc cagactggac tgcaatggca gggctctctgc	60
tcactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct ccaggttagc	120
tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg	180
gagtttcgcc atgttggcca gctgggtctca aactcctgac ctcaagcgac ctgcctgcct	240
cggcctccca aagtgtctga attataggca tgagtcaaca cgcccagcct aaagatatatt	300
t	301

97

<210> 300  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 300  
 attcagtttt atttgcctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga 60  
 tatgtcccac acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca 120  
 gctgcattcc acaaggttct cagcctaata agtttcaacta cctgccagtc tcaaaactta 180  
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgcccacc gtcttggtac 240  
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat 300  
 g 301

<210> 301  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 301  
 tttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60  
 agaggacccc aggtctccaa gcaaccacat ggtaaggggc atgaataatt aaaagttggg 120  
 gggaactcac aaagaccctc agagctgaga caccacaaac agtgggagct cacaagacc 180  
 ctgagagctg agacaccac aacagtggga gctcacaaag accctcagag ctgagacacc 240  
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300  
 t 301

<210> 302  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 302  
 aggtacacat tttagcttggt gtaaatgact cacaaaactg attttaaaat caagttaatg 60  
 tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac 120  
 ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180  
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240  
 caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg 300  
 g 301

<210> 303  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 303  
 aggtaccaac tgtggaaata ggtagaggat ctttttttct ttccatatca actaagttgt 60  
 atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac 120  
 tggctaattg aactaccgct tgcattgtaa aaatggtggg ttgtgaaatg atcataggcc 180  
 agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240  
 catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300  
 c 301

<210> 304  
 <211> 301  
 <212> DNA  
 <213> Homo sapien



## &lt;400&gt; 304

acatggatgt	tattttgcag	actgtcaacc	tgaatttcta	tttgcttgac	attgccta	60
tattagtttc	agtttcagct	taccacattt	ttgtctgcaa	catgcaraas	agacagtgcc	120
cttttttagtg	tatcatatca	ggaatcatct	cacattgggt	tgtgccatta	ctggtgcagt	180
gactttcagc	cacttgggta	aggtggagtt	ggccatatgt	ctccactgca	aaattactga	240
ttttcctttt	gtaattaata	agtgtgtgtg	tgaagattct	ttgagatgag	gtatatatct	300
c						301

&lt;210&gt; 305

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

## &lt;400&gt; 305

gangtacagc	gtggtcaagg	taacaagaag	aaaaaaatgt	gagtggcatc	ctgggatgag	60
cagggggaca	gacctggaca	gacacgttgt	catttgctgc	tgtgggtagg	aaaatgggag	120
taaaggagga	gaaacagata	caaaatctcc	aactcagtat	taaggatttc	tcatgcctag	180
aatattggta	gaaacaagaa	tacattcata	tggcaataaa	ctaaccatgg	tggaacaaaa	240
ttctgggatt	taagttggat	accaangaaa	ttgtattaaa	agagctgttc	atggaataag	300
a						301

&lt;210&gt; 306

&lt;211&gt; 8

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

## &lt;400&gt; 306

Val	Leu	Gly	Trp	Val	Ala	Glu	Leu
1				5			

&lt;210&gt; 307

&lt;211&gt; 637

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

## &lt;400&gt; 307

acagggratg	aagggaaagg	gagaggatga	ggaagcccc	ctggggattt	ggtttgggtc	60
ttgtgatcag	gtggtctatg	gggcttatcc	ctacaaagaa	gaatccagaa	ataggggcac	120
attgaggaat	gatacttgag	cccaaagagc	attcaatcat	tgttttattt	gccttmtttt	180
cacaccattg	gtgagggagg	gattaccacc	ctggggttat	gaagatgggt	gaacacccca	240
cacatagcac	cggagatatg	agatcaacag	tttcttagcc	atagagattc	acagcccaga	300
gcaggaggac	gcttgcacac	catgcaggat	gacatggggg	atgcgctcgg	gattgggtgtg	360
aagaagcaag	gactgttaga	ggcaggcttt	atagtaacaa	gacgggtggg	caaactctga	420
tttccgtggg	ggaatgtcat	ggtcttgctt	tactaaagttt	tgagactggc	aggtagtga	480
actcattagg	ctgagaacct	tgtggaatgc	acttgaccca	sctgatagag	gaagtagcca	540
gggtgggagcc	tttcccagtg	ggtgtggggac	atatctggca	agattttgtg	gcactcctgg	600
ttacagatac	tgggggcagca	aataaaaactg	aatcttg			637

&lt;210&gt; 308

&lt;211&gt; 647

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

99

<220>  
 <221> misc\_feature  
 <222> (1)...(647)  
 <223> n = A,T,C or G

<400> 308  
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60  
 tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa 120  
 ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180  
 ccacccctct gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg 240  
 ctagagaaaa gaccaacaac ggcctcaaaag gatctcttac catgaaggtc tcagctaatt 300  
 cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct 360  
 catttttgtt gtggataaag tcaggatgcc cagggggccag agcagggggc tgcttgcttt 420  
 gggacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480  
 tgatatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca 540  
 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600  
 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309  
 <211> 460  
 <212> DNA  
 <213> Homo sapien

<400> 309  
 actttatagt ttaggctgga cattggaaaa aaaaaaaagc cagaacaaca tgtgatagat 60  
 aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 120  
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180  
 accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtcg 240  
 ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctaccag 300  
 ctgggtgtgt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggttaacc 360  
 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat 420  
 ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt 460

<210> 310  
 <211> 539  
 <212> DNA  
 <213> Homo sapien

<400> 310  
 acgggactta tcaataaaag ataggaaaag aagaaaactc aaatattata ggcagaaatg 60  
 ctaaaggttt taaaatatgt caggatttga agaaggcatg gataaagaac aaagttcagt 120  
 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180  
 gtcagacagt aagattttgtg ggaatgggt tggttttgtg tatgggtatgt attttagcaa 240  
 taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgetgaa 300  
 ttcctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac 360  
 ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc aactgtgac 420  
 atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc 480  
 atattttcac ccccaaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga 539

<210> 311  
 <211> 526  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(526)  
 <223> n = A,T,C or G

100

&lt;400&gt; 311

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ttttgacgtt	ttctctaaac	tactaaagag	gcattaatga	tccataaatt	atattatcta	120
catttacagc	atttaaaatg	tgttcagcat	gaaatattag	ctacagggga	agctaaataa	180
attaaacatg	gaataaagat	ttgtccctta	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataacc	360
tctctttaca	gggagctcct	gcagccccta	cagaaatgag	tggtcgagat	tcttgattgc	420
acagcaagag	cttctcatct	aaaccctttc	cctttttagt	atctgtgtat	caagtataaa	480
agttctataa	actgtagtnt	acttatttta	atcccaaaag	cacagt		526

&lt;210&gt; 312

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(500)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 312

cctctctctc	cccaccccct	gactctagag	aactgggttt	tctcccagta	ctccagcaat	60
tcattttctga	aagcagttga	gccactttat	tccaaagtac	actgcagatg	ttcaaactct	120
ccattttctct	ttcccttcca	cctgccagtt	ttgctgactc	tcaacttgtc	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacaggc	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatttt	tcttccaaaa	tcagtaggaa	atctaaactt	atcccctctt	300
tgcagatgtc	tagcagcttc	agacatttgg	ttaagaacct	atgggaaaaa	aaaaaatcct	360
tgctaagtgt	gtttcctttg	taaaccanga	ttcttatttg	nctggtatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttggttttg	aatataggag	aaatcagttt	gctgaaaagt	480
tagtcttaat	tatctattgg					500

&lt;210&gt; 313

&lt;211&gt; 718

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(718)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 313

ggagatttgt	gtggtttgca	gccgagggag	accaggaaga	tctgcatggt	gggaaggacc	60
tgatgataca	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtgcacat	gtttttgcac	atttccagcc	cttttaataa	tccacacaca	caggaagcac	240
aaaaggaagc	acagagatcc	ctgggagaaa	tgcccgcccg	ccatcttggg	tcacgcgatga	300
gcctcgccct	gtgcctgntc	ccgcttggtga	gggaaggaca	ttagaaaaatg	aattgatgtg	360
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aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
cgttatacca	atcatttcta	tttctaccct	caaacaagct	gtngaatatc	tgacttacgg	660
ttcttntggc	ccacattttc	atnatccacc	ccntcntttt	aannttantc	caaantgt	718

&lt;210&gt; 314

101

<211> 358  
 <212> DNA  
 <213> Homo sapien

<400> 314  
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 caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa 180  
 gctctcggtg gtccagccac tgtgaaacat gtcaccttta gattaacctc gtggacgctc 240  
 ttgttgattt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttgct 300  
 tctggggcat ttccttggtg tgcagaggac caccacacag atgacagcaa tctgaatt 358

<210> 315  
 <211> 341  
 <212> DNA  
 <213> Homo sapien

<400> 315  
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 ataggtgatg atgaggacat ggaatgggcc cccaaggatg gtctgtccaa agaagcgagt 120  
 gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag cccaatgac 180  
 agtcaccagc tccccgacca gccggatgc gtccttaggg gtcattgagg ctctctgaag 240  
 tagcttctgc tgtaagaggg tggtgtcccg ggggctcgtg cggttattgg tcttgggctt 300  
 gagggggcgg tagatgcagc acatgggtgaa gcagatgatg t 341

<210> 316  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 316  
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 tgtgggctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact 120  
 cattcaggga gctctggttg caatattagt t 151

<210> 317  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 317  
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 atcttcattt atctctggcc ttaaccctgg ctcttgaggc tgcggccagc agatcccagg 120  
 ccagggtctt gttcttgcca cacctgcttg a 151

<210> 318  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 318  
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 tgggggcggg ttatcaggca gtgataaaca t 151

<210> 319  
 <211> 151  
 <212> DNA

102

&lt;213&gt; Homo sapien

&lt;400&gt; 319

```

aactagtgga tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta      60
catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg      120
taagattggg tttatgtgat tttagtgggt a                                     151

```

&lt;210&gt; 320

&lt;211&gt; 150

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 320

```

aactagtgga tccactagtc cagtgtgggt gaattccatt gtgttggggt tctagatcgc      60
gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt      120
gagtgttcta cagcttacag taaataccat                                     150

```

&lt;210&gt; 321

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 321

```

agcaactttg tttttcatcc aggttatatt aggettagga tttcctctca cactgcagtt      60
taggggtggc ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg      120
tgcctctgag aaatcaaagt cttcatacac t                                     151

```

&lt;210&gt; 322

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(151)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 322

```

atccagcadc ttctcctggt tcttgccctc ctttttcttc ttcttasatt ctgcttgagg      60
tttgggcttg gtcagtttgc cacagggtt ggagatggtg acagtcttct ggcattcggc      120
attgtgcagg gctcgttca nacttcagtt t                                     151

```

&lt;210&gt; 323

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(151)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 323

```

tgaggacttg tktctttttt ctttatattt aatcctctta ckttgtaaatt atattgccta      60
nagactcant tactaccag tttgtggttt twtgggagaa atgtaactgg acagttagct      120
gttcaatyaa aaagacactt ancccatgtg g                                     151

```

&lt;210&gt; 324

<211> 461  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(461)  
 <223> n = A,T,C or G

<400> 324

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agaagtgtgc agctaaagga atccaggttg ttggttgac tgtaataacc tttgatgaaa	120
agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact	180
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ctcatacagg gatatacaaaa taccctttgt gctaccacgg ccctggggaa tcaggtgact	300
cacacaaatg caatagttgg tcaactgcatt tttacctgaa ccaaagctaa acccggtgtt	360
gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga	420
aaaaacgcac aagagcccct gccctgccct agctgangca c	461

<210> 325  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<400> 325

acactgtttc catgttatgt ttctacacat tgctacctca gtgctcctgg aaacttagct	60
tttgaatgtc ccaagtagtc caccttcatt taactctttg aaactgtatc atctttgcca	120
agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt	180
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gttttgtttt ggactctctg tgggtccctc caatgctgtg ggtttccaac cagggaagg	300
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ctggccaagc aggtgtgttt gcaagaatga aatgaatgat	400

<210> 326  
 <211> 1215  
 <212> DNA  
 <213> Homo sapien

<400> 326

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cggagggcaa gaccagaagg actcctgcaa cgggtactct ggggggcccc tgatctgcaa	540
cgggtacttg cagggccttg tgtctttcgg aaaagcccg tgtggccaag ttggcgtgcc	600
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ttaactctgg ggactgggaa cccatgaaat tgaccccaa atacatcctg cggaaggaa	720
tcaggaatat ctgttcccg cccctcctcc ctcaggccca ggagtcagg ccccagccc	780
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104

ctttcccta gatccagaaa taaagtctaa gagaagcgca aaaaaaaaaa aaaaaaaaaa 1200  
 aaaaaaaaaa aaaaa 1215

<210> 327  
 <211> 220  
 <212> PRT  
 <213> Homo sapien

<400> 327  
 Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met  
 1 5 10 15  
 Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val  
 20 25 30  
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly  
 35 40 45  
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu  
 50 55 60  
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala  
 65 70 75 80  
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp  
 85 90 95  
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn  
 100 105 110  
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro  
 115 120 125  
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys  
 130 135 140  
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly  
 145 150 155 160  
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro  
 165 170 175  
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala  
 180 185 190  
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys  
 195 200 205  
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 210 215 220

<210> 328  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

<400> 328  
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 atccgcagtg ggtgctgtca gccacacact gttccagaa ctcctacacc atcgggctgg 180  
 gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag gcca 234

<210> 329  
 <211> 77  
 <212> PRT  
 <213> Homo sapien

<400> 329  
 Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser  
 1 5 10 15  
 Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu

105

20 25 30  
 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr  
 35 40 45  
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu  
 50 55 60  
 Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala  
 65 70 75

<210> 330  
 <211> 70  
 <212> DNA  
 <213> Homo sapien

<400> 330  
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 gctgcagcca 70

<210> 331  
 <211> 22  
 <212> PRT  
 <213> Homo sapien

<400> 331  
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu  
 1 5 10 15  
 Val Ser Gly Ser Cys Ser  
 20

<210> 332  
 <211> 2507  
 <212> DNA  
 <213> Homo sapien

<400> 332  
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 gtacatcaac tgttcagctt cctgggaaag tagttgtggt cacaggagct aatacaggta 180  
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 aggtgttggg gcggaactg gacctgtctg atactaagtc tattcgagct tttgctaagg 360  
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 acttctctct aacctatctg ctgctagaga aactaaagga atcagcccca tcaaggatag 540  
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agggagtatt	ttcacaaagt	tcaaaacagc	cacaataatc	agagatggag	caaaccagtg	1620
ccatccagtc	tttatgcaaa	tgaaatgctg	caaagggag	cagattctgt	atatgttggt	1680
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tggaagataa	tgacacaaat	gaagggacta	gttaaggatt	aactagccct	ttaaggatta	1800
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&lt;210&gt; 333

&lt;211&gt; 3030

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 333

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&lt;210&gt; 334

&lt;211&gt; 2417

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 334

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&lt;210&gt; 335

&lt;211&gt; 2984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 335

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&lt;210&gt; 336

&lt;211&gt; 147

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 336

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Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
35          40          45
Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
50          55          60
Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
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Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
85          90          95
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100          105          110
Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
115          120          125
Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
130          135          140
Ala Phe Trp
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&lt;210&gt; 337

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 337

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Ala Leu Thr Gly Phe Thr Phe Ser Ala
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&lt;210&gt; 338

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 338

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Leu Leu Ala Asn Asp Leu Met Leu Ile
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&lt;210&gt; 339

&lt;211&gt; 318

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

<400> 339  
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 Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly  
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 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu  
 65 70 75 80  
 Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val  
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 Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly  
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 Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala  
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 210 215 220  
 Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val  
 225 230 235 240  
 Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe  
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 Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu  
 260 265 270  
 Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His  
 275 280 285  
 Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg  
 290 295 300  
 Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp  
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&lt;210&gt; 340

&lt;211&gt; 483

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 340

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111

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<210> 344  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<400> 344  
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 caataggcca cataaacttg gctggatgga acctcacaat aagggtggtca cctcttggtt 120  
 gtttaggggg atgccaaaga taaggccagc tcagttatat gaagagaagc agaacaaaca 180  
 agtctttcag agaaatggat gcaatcagag tgggatcccg gtcacatcaa ggtcacactc 240  
 caccttcatg tgctgaatg gttgccaggt cagaaaaatc caccctttac gagtggggct 300  
 togacctat atcccccgcc cgcgtccctt tctccataaa attcttctta gtagctatta 360  
 ccttcttatt atttgatcta gaaattgccc tccttttacc cctaccatga gccctacaaa 420

112

caactaacct gccactaata gttatgtcat ccctcttatt aatcatcatc ctagccctaa 480  
gtctggccta tgagtgacta caaaaaggat tagactgagc cgaataacaa aaaaaa 536

<210> 345  
<211> 251  
<212> DNA  
<213> Homo sapien

<400> 345  
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tgaatgaagc ccccatcttt gtgcctcctg aaaagagagt ggaagtgtcc gaggactttg 120  
gcgtgggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga 180  
aaataacata tcggatttgg agagacactg ccaactggct ggagattaat ccggacactg 240  
gtgccatttc c 251

<210> 346  
<211> 282  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (282)  
<223> n = A,T,C or G

<400> 346  
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agggagacta tacctggctc ttgccctaag tgagaggtct tccctcccgc accaaaaaat 180  
agaaaggctt tctatttcac tggcccagggt agggggaagg agagtaactt tgagtctgtg 240  
ggtctcattt cccaagggtgc cttcaatgct catnaaaacc aa 282

<210> 347  
<211> 201  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (201)  
<223> n = A,T,C or G

<400> 347  
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tctgagactg actggaccca cccagaccca gggaagat acatgttacc atatcatctt 180  
tataaagaat ttttttttgt c 201

<210> 348  
<211> 251  
<212> DNA  
<213> Homo sapien

<400> 348  
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agagagaaca gtgccagaat gaaactgacc ctaagtccca ggtgccctg ggcaggcaga 120  
aggagacact cccagcatgg aggagggtt atcttttcat cctaggctag gtctacaatg 180  
ggggaagggt ttattataga actccaaca gccacctca ctctgtccac ccacccgatg 240

gccctgcctc c

251

&lt;210&gt; 349

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 349

taaaaatcaa gccattta	at tgtatctttg	aaggtaaaca	atatatggga	gctggatcac	60
aaccctgag gatgccagag	ctatgggtcc	agaacatggt	gtggtattat	caacagagtt	120
cagaagggtc tgaactctac	gtgttaccag	agaacataat	gcaattcatg	cattccactt	180
agcaattttg taaaatacca	gaaacagacc	ccaagagtct	ttcaagatga	ggaaaaatca	240
actcctggtt t					251

&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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agcccgcccg gtgaagctcg	ctgctttccc	tacctcctta	agtgactgcc	aaacgcccac	120
cggctggaat tgctctggtt	atgatgacag	agaaaatgat	ctcttcctct	gtgacaccaa	180
cacctgtaaa tttgatggg	aatgtttaag	aattggagac	actgtgactt	gcgtctgtca	240
gttcaagtgc aacaatgact	atgtgcctgt	gtgtggctcc	aatggggaga	gctaccagaa	300
tgagtgttac ctgagcagag	ctgcatgcaa	acagcagagt	gagatacttg	tggtgtcaga	360
aggatcatgt gccacagtcc	atgaaggctc	tgagaaaact	agtcaaaagg	agacatccac	420
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catgtctttg ggtcgatgtc	aagataaac	aactacaact	actaagtctg	aagatgggca	660
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aatcgag					908

&lt;210&gt; 351

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

ccagttatatt gcaagtggta	agagcctatt	taccataaat	aatactaaga	accaaactcaa	60
gtcaaacctt aatgccattg	ttattgtgaa	ttaggattaa	gtagtaattt	tcaaaattca	120
cattaacttg attttaaaat	cagwtttgyg	agtcattttac	cacaagctaa	atgtgtacac	180
tatgataaaa acaaccattg	tattcctgtt	tttctaaaca	gtcctaattt	ctaactgt	240
atatatcctt cgacatcaat	gaactttgtt	ttcttttact	ccagtaataa	agtaggcaca	300
gatctgtcca caacaaactt	gccctctcat	gccttgctc	tcacatgct	ctgctccagg	360
tcagccccct tttggcctgt	ttgttttgtc	aaaaacctaa	tctgcttctt	gcttttcttg	420
gtaatatata tttagggaag	atgttgcttt	gccacacac	gaagcaaagt	aa	472

&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352



114

ctcaaagcta	atctctcggg	aatcaaacca	gaaaaggcca	aggatccttag	gcatggtgga	60
tgtggataag	gccaggtcaa	tggctgcaag	catgcagaga	aagaggtaca	tcggagcgtg	120
caggctgcgt	tccgtcctta	cgatgaagac	cacgatgcag	tttccaaaca	ttgccactac	180
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ataagcaca	a					251

<210> 353  
 <211> 436  
 <212> DNA  
 <213> Homo sapien

<400> 353						
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gtatccaaaa	gcaaaacagc	agatatacaa	aattaaagag	acagaagata	gacattaaca	180
gataaggcaa	cttatacatt	gacaatccaa	atccaataca	tttaaacatt	tgaggaaatga	240
gggggacaaa	tggaagccar	atcaaatttg	tgtaaaacta	ttcagtatgt	ttcccttgct	300
tcatgtctga	raaggctctc	ccttcaatgg	ggatgacaaa	ctccaaatgc	cacacaaatg	360
ttacacagaat	actagattca	cactggaacg	ggggtaaaga	agaaattatt	ttctataaaa	420
gggctcctaa	tgtagt					436

<210> 354  
 <211> 854  
 <212> DNA  
 <213> Homo sapien

<400> 354						
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caagtctgaa	accaaatcta	ggaaacatag	gaaacgagcc	aggcacaggg	ctgggtggcc	120
atcagggacc	accctttggg	ttgatatttt	gcttaactctg	catcttttga	gtaagatcat	180
ctggcagtag	aagctgttct	ccagggtacat	ttctctagct	catgtacaaa	aacatcctga	240
aggactttgt	cagggtgcctt	gctaaaagcc	agatgcggtc	ggcacttcct	tggtctgagg	300
ttaattgcac	acctacagcc	actgggctca	tgctttcaag	tattttgtcc	tcactttagg	360
gtgagtgaag	gatccccatt	ataggagcac	ttgggagaga	tcataataaa	gctgactctt	420
gagtacatgc	agtaattggg	tagatgtgtg	tggtgtgtct	tcattcctgc	aagggtgctt	480
gttagggagt	gtttccagga	ggaacaagtc	tgaaaccaat	catgaaataa	atggtaggtg	540
tgaactggaa	aactaatcca	aaagagagat	cgtgatatca	gtgtgggtga	tacaccttgg	600
caatatggaa	ggctctaatt	tgcccatatt	tgaaataata	attcagcttt	ttgtaataca	660
aaataacaaa	ggattgagaa	tcatgggtgc	taatgtataa	aagacccagg	aaacataaat	720
atatcaactg	cataaatgta	aaatgcattg	gacccaagaa	ggccccaag	tggcagacaa	780
cattgtaccc	attttccctt	ccaaaatgtg	agcggcgggc	ctgctgcttt	caaggctgtc	840
acacgggatg	tcag					854

<210> 355  
 <211> 676  
 <212> DNA  
 <213> Homo sapien

<400> 355						
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cagggtcaaag	ctgatctttc	tggaatgtca	ccaaccaagg	gcctatattt	atcaaaagcc	120
atccacaagt	catacctgga	tgtcagcgaa	gagggcacgg	aggcagcagc	agccactggg	180
gacagcatcg	ctgtaaaaaa	cctaccaatg	agagctcagt	tcaaggcgaa	ccacccttc	240
ctgttcttta	taaggcacac	tcataccaac	acgatcctat	tctgtggcaa	gcttgccctt	300
ccctaatacag	atgggggtga	gtaaggctca	gagttgcaga	tgaggtgcag	agacaatcct	360
gtgactttcc	cacggccaaa	aagctgttca	cacctcacgc	acctctgtgc	ctcagtttgc	420
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tttgtaatac	atggaaaaag	gtagacttat	gcagaaagcc	tttctggctt	tcttatctgt	540

115

ggtgtctcat	ttgagtgtctg	tccagtgaca	tgatcaagtc	aatgagtaaa	attttaaggg	600
attagatttt	cttgacttgt	atgtatctgt	gagatcttga	ataagtgacc	tgacatctct	660
gcttaaagaa	aaccag					676

<210> 356  
 <211> 574  
 <212> DNA  
 <213> Homo sapien

<400> 356						
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catgtggcac	ctgactggca	tcaaaccaaa	gttcgtaggc	caacaaagat	gggccactca	120
caagctcccc	attttagat	ctcagtgcc	atgagtatct	gacacctgtt	cctctcttca	180
gtctcttagg	gaggcttaaa	tctgtctcag	gtgtgctaag	agtgccagcc	caaggkgtc	240
aaaagtccac	aaaactgcag	tctttgctgg	gatagtaagc	caagcagtgc	ctggacagca	300
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ttcttctgtc	tctgcctaga	ctggaataaa	aagccaatct	ctctcgtggc	acagggaagg	420
agatacaagc	tcgtttacat	gtgatagatc	taacaaaggc	atctaccgaa	gtctggtctg	480
gatagacggc	acaggggagct	cttaggtcag	cgctgctgg	tggaggacat	tcctgagtcc	540
agctttgcag	cctttgtgca	acagtacttt	ccca			574

<210> 357  
 <211> 393  
 <212> DNA  
 <213> Homo sapien

<400> 357						
tttttttttt	tttttttttt	tttttttttt	tacagaatat	aratgcttta	tactgkact	60
taatatggkg	kcttyttcac	tatacttaaa	aatgcaccac	tcataaatat	ttaattcagc	120
aagccacaac	caaracttga	ttttatcaac	aaaaaccct	aatataaac	ggsaaaaaag	180
atagatataa	ttattccagt	ttttttaaaa	cttaaaarat	attccattgc	cgaattaara	240
araarataag	tgttatatgg	aaagaagggc	attcaagcac	actaaaraaa	cctgaggkaa	300
gcataatctg	tacaaaatta	aactgtcctt	tttggcattt	taacaaattt	gcaacgktct	360
tttttttctt	tttctgtttt	tttttttttt	tac			393

<210> 358  
 <211> 630  
 <212> DNA  
 <213> Homo sapien

<400> 358						
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gcatagagta	gggaagctaa	tccagcacag	ggaggtcaca	gagacatccc	taaggaagtg	180
gagtttaaac	tgagagaagc	aagtgcctaa	actgaaggat	gtgttgaa	agaagggaga	240
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gaaagagagc	tagaacagct	ggagccgttc	tccggtgtaa	agaggagtca	aagagataag	360
attaaagatg	tgaagattaa	gatcttggtg	gcattcaggg	attggcactt	ctacaagaaa	420
tactgaagg	gagtaatgtg	acattacttt	tcacttcagg	atggccattc	taactccagg	480
gggtagactg	gactaggtaa	gactggaggc	aggtagacct	cttctaaggc	ctgcatagtg	540
gaaagacaaa	aataagtggg	gaaattcagg	ggatagttaa	aatcagtagg	acttaatgag	600
caagccagag	gttctctccac	aacaaccagt				630

<210> 359  
 <211> 620  
 <212> DNA  
 <213> Homo sapien

<400> 359  
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 aaagacaaca tgataacctta ggaagcaaca ctaccctttc aggcataaaa tttggagaaa 360  
 tgcaacatta tgcttcatga ataatatgta gaaagaaggt ctgatgaaaa tgacatcctt 420  
 aatgtaagat aactttataa gaattctggg tcaataaaaa ttctttgaag aaaacatcca 480  
 aatgtcattg acttatcaaa tactatcttg gcatataacc tatgaaggca aaactaaaca 540  
 aacaaaaagc tcacaccaa caaaaccatc aacttatttt gtattctata acatacgaga 600  
 ctgtaaagat gtgacagtgt 620

<210> 360  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<400> 360  
 aaaaaaaaa agccagaaca acatgtgata gataatatga ttggctgcac acttcagac 60  
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 tactcatcat ttttgccag cagttgtttg atcaccacac atcatgccag aatactcagc 180  
 aaaccttctt agctcttgag aagtcaaaagt ccgggggaat ttattcctgg caattttaat 240  
 tggactcctt atgtgagagc agcggctacc cagctggggt ggtggagcga acccgtcact 300  
 agtggacatg cagtggcaga gctcctggta accacctaga ggaatacaca ggcacatgtg 360  
 tgatgccaag cgtgacacct gtagcactca aatttgtctt gttttgtctt ttcggtgtgt 420  
 agattcttag t 431

<210> 361  
 <211> 351  
 <212> DNA  
 <213> Homo sapien

<400> 361  
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 caatcctgga ttcaatgtct gaaacctcgc tctctgcctg ctggacttct gaggccgtca 300  
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<210> 362  
 <211> 463  
 <212> DNA  
 <213> Homo sapien

<400> 362  
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 ccccggtcac agaaatgacc aggttgggtg ttttcagggt ccagtctgg gtcagcagct 180  
 cgtaaaggat ttccgcgtcc gtgtgcagg acagacgtat ataactccct ttcttcccca 240  
 gtgtctcaaa ctgaatatcc ccaaggcgt cgtaggaaa ttcttgggtg tgtttcttgt 300  
 agttccattt ctcacttttg ttgatctggg tgccttccat gtgctggctc tgggcatagc 360  
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 ttgagcctgc ttatggaaac tggattgtt agcttaata gac 463

<210> 363  
 <211> 653

117

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(653)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 363

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ctcttgngga	ttctgggtga	catcttcatg	aatggcaacc	gtgccagwga	ggctgtcctc	120
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ntgggccctg	gagctgggat	gacattgagt	ttgagctgct	gacctgggat	gaggaaggag	540
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cccgcctcag	attccctcag	acctttgccg	gtcccattat	tggtcstggt	ggt	653

&lt;210&gt; 364

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 364

actagaggaa	agacgttaaa	ccactctact	accacttgtg	gaactctcaa	agggtaaatg	60
acaaagccaa	tgaatgactc	taaaaacaat	atttacattt	aatggtttgt	agacaataaa	120
aaaacaaggt	ggatagatct	agaattgtaa	cattttaaga	aaaccatagc	atttgacaga	180
tgagaaagct	caattataga	tgcaaagtta	taactaaact	actatagtag	taaagaaata	240
catttcacac	ccttcatata	aattcactat	cttggttga	ggcactccat	aaaatgtatc	300
acgtgcatag	taaatcttta	tatttgctat	ggcgttgac	tagaggactt	ggactgcaac	360
aagtggatgc	gcggaaaatg	aaatcttctt	caatagccca	g		401

&lt;210&gt; 365

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 365

ccagtgtcat	atttgggctt	aaaatttcaa	gaagggcact	tcaaattggct	ttgcatttgc	60
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&lt;210&gt; 366

&lt;211&gt; 1851

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 366

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caaattacat	gatgatgact	agaacagca	tactctctgg	ccgtctttcc	agatcttgag	300
aagatacatc	aacattttgc	tcaagtagag	ggctgactat	acttgctgat	ccacaacata	360
cagcaagtat	gagagcagtt	cttccataatc	tatccagcgc	atttaaattc	gcttttttct	420
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atttatcttc	attgtagaca	gcatagtgtg	gagtggtatt	tccatactca	tctggaatat	600
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&lt;210&gt; 367

&lt;211&gt; 668

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 367

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&lt;210&gt; 368

&lt;211&gt; 1512

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 368

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&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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120

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<210> 370

<211> 2184

<212> DNA

<213> Homo sapien

<400> 370

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<210> 371

<211> 1855

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

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<400> 371

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&lt;210&gt; 372

&lt;211&gt; 1059

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 372

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&lt;210&gt; 373

&lt;211&gt; 1155



&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 373

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&lt;210&gt; 374

&lt;211&gt; 2000

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 374

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tggtgctgcc	actgcttccc	ctgctgcagg	gggagcggca	agagcaaggt	gggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccaggtacc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctggtgggg	aaagtcccca	gaaaggatct	catcgctcatg	480
ctcagggaca	ctgacgtgaa	caagaaggac	aagcaaaaaga	ggactgctct	acatctggcc	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcca	ggaagatgaa	660
tgtgcgttaa	tggtgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
tatggtgctg	atatcgaatc	aaaaaacaag	catggcctca	caccactggt	acttggtgta	840
catgagcaaa	aacagcaagt	cgtgaaat	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
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gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggacagacg	1020
gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaca	agacttaaag	1140
ctgacatcag	aggaagagtc	acaaagggtc	aaaggcagtg	aaaatagcca	gccagagaaa	1200
atgtctcaag	aaccagaaat	aaataaggat	ggtgatagag	agggtgaaga	agaaatgaag	1260
aagcatgaaa	gtaataatgt	gggattacta	gaaaacctga	ctaattggtg	cactgctggc	1320
aatggtgata	atggattaat	tcctcaaagg	aagagcagaa	cacctgaaaa	tcagcaattt	1380
cctgacaacg	aaagtgaaga	gtatcacaga	atttgcgaa	tagtttctga	ctacaaagaa	1440
aaacagatgc	caaaatactc	ttctgaaaac	agcaaccacg	aacaagactt	aaagctgaca	1500
tcagaggaag	agtcacaaa	gcttgagggc	agtgaaaatg	gccagccaga	gctagaaaat	1560
tttatggcta	tcgaagaaat	gaagaagcac	ggaagtactc	atgtcggatt	cccagaaaa	1620

123

ctgactaatg	gtgccactgc	tggcaatggt	gatgatggat	taattcctcc	aaggaagagc	1680
agaacacctg	aaagccagca	atttcctgac	actgagaatg	aagagtatca	cagtgcagaa	1740
caaaatgata	ctcagaagca	atthttgtgaa	gaacagaaca	ctggaatatt	acacgatgag	1800
attctgattc	atgaagaaaa	gcagatagaa	gtggttgaaa	aaatgaattc	tgagctttct	1860
cttagttgta	agaaagaaaa	agacatcttg	catgaaaata	gtacgttgcg	ggaagaaatt	1920
gccatgctaa	gactggagct	agacacaatg	aaacatcaga	gccagctaaa	aaaaaaaaaa	1980
aaaaaaaaaa	aaaaaaaaaa					2000

<210> 375  
 <211> 2040  
 <212> DNA  
 <213> Homo sapien

<400> 375						
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aggagcaaga	tgggcaagtg	gtgctgccgt	tgcttcccct	gctgcaggga	gagcggcaag	120
agcaacgtgg	gcacttctgg	agaccacgac	gactctgcta	tgaagacact	caggagcaag	180
atgggcaagt	ggtgccgcca	ctgcttcccc	tgctgcaggg	ggagtggcaa	gagcaacgtg	240
ggcgcttctg	gagaccacga	cgactctgct	atgaagacac	tcaggaaaca	gatgggcaag	300
tggtgctgcc	actgcttccc	ctgctgcagg	gggagcggca	agagcaaggt	ggcgcttgg	360
ggagactacg	atgacagtgc	cttcatggag	cccagggtacc	acgtccgtgg	agaagatctg	420
gacaagctcc	acagagctgc	ctggtggggg	aaagtcccca	gaaaggatct	catcgctcatg	480
ctcagggaca	ctgacgtgaa	caagaaggac	aagcaaaaga	ggactgctct	acatctggcc	540
tctgccaatg	ggaattcaga	agtagtaaaa	ctcctgctgg	acagacgatg	tcaacttaat	600
gtccttgaca	acaaaaagag	gacagctctg	ataaaggccg	tacaatgcc	ggaagatgaa	660
tgtgcgttaa	tggtgctgga	acatggcact	gatccaaata	ttccagatga	gtatggaaat	720
accactctgc	actacgctat	ctataatgaa	gataaattaa	tggccaaagc	actgctctta	780
tatggtgctg	atatcgaaat	aaaaaacaag	catggcctca	caccactgtt	acttgggtgta	840
catgagcaaa	aacagcaagt	cgtgaaatth	ttaatcaaga	aaaaagcgaa	tttaaatgca	900
ctggatagat	atggaaggac	tgctctcata	cttgcgtgat	gttgtggatc	agcaagtata	960
gtcagccttc	tacttgagca	aaatattgat	gtatcttctc	aagatctatc	tggacagacg	1020
gccagagagt	atgctgtttc	tagtcatcat	catgtaatth	gccagttact	ttctgactac	1080
aaagaaaaac	agatgctaaa	aatctcttct	gaaaacagca	atccagaaca	agacttaaa	1140
ctgacatcag	aggaagagtc	acaaagggtc	aaaggcagtg	aaaatagcca	gccagagaaa	1200
atgtctcaag	aaccagaaat	aaataaggat	ggtgatagag	aggttgaa	agaaatgaag	1260
aagcatgaaa	gtaataatgt	gggattacta	gaaaacctga	ctaattggtg	cactgctggc	1320
aatggtgata	atggattaat	tcctcaaaag	aagagcagaa	cacctgaaaa	tcagcaatth	1380
cctgacaacg	aaagtgaaga	gtatcacaga	atthgcgaat	tagtttctga	ctacaaagaa	1440
aaacagatgc	caaaatactc	ttctgaaaac	agcaaccag	aacaagactt	aaagctgaca	1500
tcagaggaag	agtcacaaag	gcttgagggc	agtgaaaatg	gccagccaga	gaaaagatct	1560
caagaaccag	aaataaataa	ggatggtgat	agagagctag	aaaattttat	ggctatcgaa	1620
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actgctggca	atggtgatga	tggattaatt	cctccaagga	agagcagaac	acctgaaagc	1740
cagcaatthc	ctgacactga	gaatgaagag	tatcacagtg	acgaacaaaa	tgatactcag	1800
aagcaatthc	gtgaagaaca	gaacactgga	atattacacg	atgagattct	gattcatgaa	1860
gaaaagcaga	tagaagtggg	tgaaaaaatg	aattctgagc	tttctcttag	ttgtaagaaa	1920
gaaaagacga	tcttgcatga	aaatagtacg	ttgcgggaag	aaattgccat	gctaagactg	1980
gagctagaca	caatgaaaca	tcagagccag	ctaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	2040

<210> 376  
 <211> 329  
 <212> PRT  
 <213> Homo sapien

<400> 376															
Met	Asp	Ile	Val	Val	Ser	Gly	Ser	His	Pro	Leu	Trp	Val	Asp	Ser	Phe
1				5					10					15	
Leu	His	Leu	Ala	Gly	Ser	Asp	Leu	Leu	Ser	Arg	Ser	Leu	Met	Ala	Glu

124

20 25 30  
 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser  
 35 40 45  
 Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg  
 50 55 60  
 Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val  
 65 70 75 80  
 Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val  
 85 90 95  
 Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr  
 100 105 110  
 His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp  
 115 120 125  
 Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp  
 130 135 140  
 Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser  
 145 150 155 160  
 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys  
 165 170 175  
 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala  
 180 185 190  
 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly  
 195 200 205  
 Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr  
 210 215 220  
 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr  
 225 230 235 240  
 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu  
 245 250 255  
 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys  
 260 265 270  
 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu  
 275 280 285  
 Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu  
 290 295 300  
 Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu  
 305 310 315 320  
 Ser Met Leu Phe Leu Val Ile Ile Met  
 325

&lt;210&gt; 377

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(148)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 377

Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile  
 1 5 10 15  
 Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys  
 20 25 30  
 Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys  
 35 40 45  
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu

125

50                      55                      60  
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp  
 65                      70                      75                      80  
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp  
                     85                      90                      95  
 Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
                     100                      105                      110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
                     115                      120                      125  
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser  
                     130                      135                      140  
 Lys Asn Lys Val  
 145

<210> 378  
 <211> 1719  
 <212> PRT  
 <213> Homo sapien

<400> 378  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
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 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
                     20                      25                      30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
                     35                      40                      45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
                     50                      55                      60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65                      70                      75                      80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
                     85                      90                      95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
                     100                      105                      110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
                     115                      120                      125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
                     130                      135                      140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145                      150                      155                      160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
                     165                      170                      175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
                     180                      185                      190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
                     195                      200                      205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210                      215                      220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225                      230                      235                      240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
                     245                      250                      255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
                     260                      265                      270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
                     275                      280                      285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
                     290                      295                      300

Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys  
 370 375 380  
 Pro Arg Thr His Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser  
 385 390 395 400  
 Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys  
 405 410 415  
 Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly  
 420 425 430  
 Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys  
 435 440 445  
 Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly  
 450 455 460  
 Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys  
 465 470 475 480  
 Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys  
 485 490 495  
 Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp  
 500 505 510  
 Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu  
 515 520 525  
 Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp  
 530 535 540  
 Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln  
 545 550 555 560  
 Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val  
 565 570 575  
 Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn  
 580 585 590  
 Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu  
 595 600 605  
 Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp  
 610 615 620  
 Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys  
 625 630 635 640  
 Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys  
 645 650 655  
 Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys  
 660 665 670  
 Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala  
 675 680 685  
 Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly  
 690 695 700  
 Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser  
 705 710 715 720  
 Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser  
 725 730 735  
 His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln  
 740 745 750  
 Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys  
 755 760 765

Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser  
 770 775 780  
 Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp  
 785 790 795 800  
 Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly  
 805 810 815  
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn  
 820 825 830  
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe  
 835 840 845  
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser  
 850 855 860  
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn  
 865 870 875 880  
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu  
 885 890 895  
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile  
 900 905 910  
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn  
 915 920 925  
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro  
 930 935 940  
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu  
 945 950 955 960  
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe  
 965 970 975  
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His  
 980 985 990  
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser  
 995 1000 1005  
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu  
 1010 1015 1020  
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His  
 1025 1030 1035 1040  
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met  
 1045 1050 1055  
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met  
 1060 1065 1070  
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys  
 1075 1080 1085  
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr  
 1090 1095 1100  
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys  
 1105 1110 1115 1120  
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp  
 1125 1130 1135  
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His  
 1140 1145 1150  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp  
 1155 1160 1165  
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg  
 1170 1175 1180  
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val  
 1185 1190 1195 1200  
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys  
 1205 1210 1215  
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly  
 1220 1225 1230

Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn  
 1235 1240 1245  
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys  
 1250 1255 1260  
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro  
 1265 1270 1275 1280  
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr  
 1285 1290 1295  
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp  
 1300 1305 1310  
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val  
 1315 1320 1325  
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala  
 1330 1335 1340  
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala  
 1345 1350 1355 1360  
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn  
 1365 1370 1375  
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr  
 1380 1385 1390  
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr  
 1395 1400 1405  
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu  
 1410 1415 1420  
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly  
 1425 1430 1435 1440  
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn  
 1445 1450 1455  
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser  
 1460 1465 1470  
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly  
 1475 1480 1485  
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu  
 1490 1495 1500  
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys  
 1505 1510 1515 1520  
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser  
 1525 1530 1535  
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu  
 1540 1545 1550  
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser  
 1555 1560 1565  
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe  
 1570 1575 1580  
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe  
 1585 1590 1595 1600  
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly  
 1605 1610 1615  
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro  
 1620 1625 1630  
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln  
 1635 1640 1645  
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile  
 1650 1655 1660  
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser  
 1665 1670 1675 1680  
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn  
 1685 1690 1695

129

Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr  
 1700 1705 1710

Met Lys His Gln Ser Gln Leu  
 1715

&lt;210&gt; 379

&lt;211&gt; 656

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 379

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu



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      370      375      380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385      390      395      400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
      405      410      415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
      420      425      430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
      435      440      445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
      450      455      460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465      470      475      480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
      485      490      495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
      500      505      510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
      515      520      525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
      530      535      540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545      550      555      560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
      565      570      575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
      580      585      590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
      595      600      605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
      610      615      620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625      630      635      640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
      645      650      655

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<210> 380
<211> 671
<212> PRT
<213> Homo sapien

```

```

<400> 380
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1      5      10      15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
      20      25      30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
      35      40      45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
      50      55      60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65      70      75      80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
      85      90      95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
      100      105      110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
      115      120      125

```

Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
130						135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155					160
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165					170						175
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
			180				185						190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
	195						200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
210						215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235					240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
				245					250						255
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
			260				265						270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
		275					280					285			
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
290						295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340				345						350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355				360						365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
370					375						380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390					395					400
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405					410					415	
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
			420				425					430			
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
		435				440						445			
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
		450				455					460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465					470					475					480
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
				485					490					495	
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu
			500					505				510			
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp
		515					520					525			
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys
					530		535				540				
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala
545					550					555					560
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg
				565					570					575	
Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His
			580					585					590		

132

Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn  
 595 600 605  
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile  
 610 615 620  
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys  
 625 630 635 640  
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala  
 645 650 655  
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
 660 665 670

<210> 381  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 381  
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa 60  
 ggtaacatgc ttcccctaag ggtatcccaa cccagggggc tcaccatgac ctctgagggg 120  
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggaccca ggactcacac 180  
 atcctggggc tccaaggcag aggagaggggt cctcaagaag gtcaggagga aaatccgtaa 240  
 caagcagtea g 251

<210> 382  
 <211> 3279  
 <212> DNA  
 <213> Homo sapiens

<400> 382  
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 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtg 120  
 cactgggagg ggacatcctg cagaaggtag gtagtagcaa acaccgctg caggggaggg 180  
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggaggag 240  
 gggcctggag ggcgtgagga ggagcagagg ggctgcattg ctggagttag ggatcagggg 300  
 caggggcgca gatggcctca cacagggaag agaggggccc tctgcaggg cctcacctgg 360  
 gccacaggag gacactgctt ttctctgag gtagcaggag ctgtggatgg tgctggacag 420  
 aagaaggaca gggcctggct cagggtgtcca gaggctgtcg ctggcttccc ttgggatca 480  
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540  
 gtggctccag gccttgcctc tgctggggcc ctacccagc ctccctcaca gtctcctggc 600  
 cctcagtctc tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660  
 gaactgacca taccagccc tgcccacggc cctccatggc tcccgaatgc cctggagagg 720  
 ggacatctag tcagagagta gtccctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780  
 gcatectgca gatgttccc gcccctcatc tgctgacctg tctgcaggga ctgtctcct 840  
 ggaccttgcc ccttgtgcag gactgggacc ctgaagtccc ctcccatag gccaagactg 900  
 gagccttgct ccctctgttg gactccctgc ccatattctt gtgggagtggt gttctggaga 960  
 catttctgtc tgttctctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020  
 agagatggag ttgcctaggc agttattggg gccaatctt ctactgtgt ctctcctcct 1080  
 ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggtatcac 1140  
 atcatggggc cctgagccat gtgcccctgcc tgaaaagcct gctgtgtaca ccaaggtggt 1200  
 gcattaccgg aagtggatca aggacacat cgcagccaac ccctgagtgc ccctgtccca 1260  
 cccctacctc tagtaaatat aagtccacct cacgttctgg catcacttgg cctttctgga 1320  
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 tgtttgtggg gtgcagagat gggaggggtg gggcccaccc tggaagagtg gacagtga 1620  
 caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680  
 acacacagca aggttgacgc tgtaaacata gccacgctg tcctgggggc actgggaagc 1740

```

ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgttggtg aaggaggagc 1800
tagggggaga aactgaaagc tgattaatta caggagggtt gttcagggtcc cccaaaccac 1860
cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
ttattatggt ttgttacatt gataggatac atactgaaat cagcaaacaa aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040
tttactaagt tttcagactg gcaggaagtc aaacctatta ggctgaggac cttgtggagt 2100
gtagctgatac cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
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gtgtccaggg tttttactgg gggctctgtg gacgagtatg gagtacttga ataattgacc 2340
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ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaagga atcaaatgtc 2520
atctcccagg agttattcaa gggtagagccc tttacttggg atgtacaggc tttgagcagt 2580
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atcattgttt tatttgcctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820
gttatgaaga tggttgaaca cccacacat agcaccggag atatgagatc aacagtttct 2880
tagccataga gattcacagc ccagagcagg aggacgctgc acaccatgca ggatgacatg 2940
ggggatgcgc tcgggatttg tgtgaagaag caaggactgt tagaggcagg ctttatagta 3000
acaagacggg ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccagggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctgggttacag atactggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt 3279

```

&lt;210&gt; 383

&lt;211&gt; 154

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

```

Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5              10              15
Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20              25              30
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35              40              45
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50              55              60
Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65              70              75              80
Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85              90              95
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100             105             110
Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115             120             125
Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130             135             140
Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145             150

```

&lt;210&gt; 384

&lt;211&gt; 557

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<400> 384  
 ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60  
 aaagatgtgt tttgttttg actctctgtg gtcccttcca atgctgtggg ttccaacca 120  
 ggggaagggt cccttttgca ttgccaagt ccataaccat gagcactact ctaccatggt 180  
 tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240  
 acttaacctt gaaatggaaa gtcttgcaat ccatttgca ggatccgtct gtgcacatgc 300  
 ctctgtagag agcagcattc ccaggacact tggaaacagt tggcactgta aggtgcttgc 360  
 tccccagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420  
 ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480  
 tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtataaa 540  
 aaaaaaaaa aaaaaaa 557

<210> 385  
 <211> 337  
 <212> DNA  
 <213> Homo sapiens

<400> 385  
 ttcccagggt atgtgagagg gaagacacat ttactatcct tgatggggct gattccttta 60  
 gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120  
 tctcaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180  
 aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240  
 tatcagacag gtccagtttc cgcaccaaca cctgctgggt ccctgtcgtg gtctggatct 300  
 ctttgccac caattcccc tttccacat ccggca 337

<210> 386  
 <211> 300  
 <212> DNA  
 <213> Homo sapiens

<400> 386  
 gggcccgcta ccggcccagg cccgcctcg cgagtcctcc tccccgggtg cctgcccga 60  
 gccgcctcgg ccagagggt gggcgoggg ctgcctctac cggctggcgg ctgtaactca 120  
 gcgaccttgg ccgaaggct ctagcaagga ccaccgacc ccagcccgcg cggcgccggc 180  
 ggggactttg cccggtgtgt gggcgggagc ggactgctgt tccgcgagc ggagcgaag 240  
 atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387  
 <211> 537  
 <212> DNA  
 <213> Homo sapiens

<400> 387  
 gggccgagtc gggcaccaag ggactctttg caggcttcct tctcggatc atcaaggctg 60  
 cccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120  
 tgaaccagga ccggttctg ggcggtgaa aggggcaagg aggcaaggac cccgtctctc 180  
 ccacggatgg ggagaggga ggaggagacc cagccaagt ccttttctc agcactgagg 240  
 gagggggtt gtttccctc cctccggcg acaagctcca gggcagggct gtccctctgg 300  
 gcggcccagc acttctcag acacaacttc ttctgctgc tccagctgtg gggatcatca 360  
 cttaccacc cccaagttc aagacaaat cttccagctg ccccttctg gtttccctgt 420  
 gtttctgtga gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg ttagtctcc 480  
 ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaa aaaaaa 537

<210> 388  
 <211> 520  
 <212> DNA  
 <213> Homo sapiens

&lt;400&gt; 388

```

aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgagggttaa ccagtttgca ttcccctaata gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaaagtga 180
ggacccccct cccaacatgc ccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttgtg gacctcacca gagaccagga ggggttggtt agctcacagg 300
acttccccca ccccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360
tcataactca ttgatgggta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
atctttcttc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tgggtgggtt ttttcttgt 520

```

&lt;210&gt; 389

&lt;211&gt; 365

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 389

```

cgttgcccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120
aacgactttc caataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgttccc tctcaccgac ctgtcctcac agctgagact 240
cccaggaaac cttcagacta ccttctctcg ccttcagcaa ggggctgtgc ccacattctc 300
tgagggctcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag 365

```

&lt;210&gt; 390

&lt;211&gt; 221

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(221)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 390

```

tgcctctcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggnnt ctcatgggtg tggaacatct ctgcttgccg ttccaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg aggagtttag gctggatttc a 221

```

&lt;210&gt; 391

&lt;211&gt; 325

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(325)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 391

```

tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgccgc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgmgctct 180
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtacc tgtcccgacg tctctaccta ccagtacgat 300

```

gagacctccg gctactacta tgacc

325

&lt;210&gt; 392

&lt;211&gt; 277

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(277)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 392

```

atattgttta actccttcct ttatatcttt taacattttc atggngaaag gttcacatct 60
agtctcactt nggcnaagnn ctctacttg agtctcttcc cgggcctgmn ccagtnghaa 120
antaccanga accgmcatgn cttanaaen ncctgggttn tgggttnntc aatgactgca 180
tgcaagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277

```

&lt;210&gt; 393

&lt;211&gt; 566

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 393

```

actagtccag tgtggtggaa ttccggcccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaaagt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgctggca 180
gagaagggtct agtttgtcca tcagcattat catgatata ggactgggta cttggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttgga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaaact 420
ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttggtg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagtattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa 566

```

&lt;210&gt; 394

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(384)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 394

```

gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatng gaccgggcca aggtggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgct actgtagacc ccaaatacca 180
tccaagatt atcgggagaa agggggcagt aattacccaa atccggttg agcatgacgt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggacaaa ttaccatcac 300
agggtagcaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt 384

```

&lt;210&gt; 395

&lt;211&gt; 399

&lt;212&gt; DNA

<213> Homo sapiens

<400> 395

```
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tattcagagg ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctcaactacag acctctgacc atgggacggt 360
gcagcctggt gagaccatcc aatoccaaata aaaatgcac 399
```

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```
tggagtnttc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacatthttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtgagg gataaaagaa ggaaaaaag aagagtgaga aaacctatth 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt 403
```

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

```
actagtnacg tgtggtggaa ttgcggcccg cgtcgacctc naanccatct ctatagcaaa 60
tccatccccg ctctggttg gtnacagaat gactgacaaa 100
```

<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 398

```
gcggccgcgt cgacagcagt tccgccagcg ctgcgccctg ggtggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgagggtg actcatcatg 180
```



138

ctccgggag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240  
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399  
<211> 298  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(298)  
<223> n = A,T,C or G

<400> 399  
acggagggtg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60  
gggggtgccng catggagcgc atgggcccgc gcctgggcca cggcatggat cgcgtgggct 120  
ccgagatcga gcgcatgggc ctggatcatgg accgcatggg ctccgtggag cgcgtgggct 180  
ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggcctccanc attgancgca 240  
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcgtggg 298

<210> 400  
<211> 548  
<212> DNA  
<213> Homo sapiens

<400> 400  
acatcaacta cttcctcatt ttaaggatg gcagttccct tcctccctt ttcctgcctt 60  
gtacatgtac atgtatgaaa ttctctctc ttaccgaact ctctccacac atcacaagggt 120  
caaagaacca cagccttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180  
tgagtctctt tttccacgt ttaaggggccc atggcaggac ttagagttgc gagttaagac 240  
tgagaggggc tagagaatta ttcatcacag gctttgaggc caccatgtc acttatcccg 300  
tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360  
gttgccccca taattctggg cctttgttgt ttgttttaac tacttgggca tcccaggaag 420  
ctttccagtg atctctacc atgggcccc ctctgggat caagcccctc ccaggccctg 480  
tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tccattggg 540  
agcagggt 548

<210> 401  
<211> 355  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(355)  
<223> n = A,T,C or G

<400> 401  
actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60  
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120  
taagagtgtt ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180  
tataaatgaa tggctgaag caaagtcccc atgggtggcg cgaagaagan aaagatgtgt 240  
ttgtttttg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300  
cccttttgca ttgccaagt ccataaccat gagcactact ctaccatggn tctgc 355

<210> 402  
<211> 407  
<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

```
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatat ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag cagggtgttc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaagggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa ttgctgagg 300
ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgatattg ctgacaactc cttttctgaa gttttactca tttccaa 407
```

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

```
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcaccaaa 60
tcctaagcaa gagcctatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgctatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga 303
```

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

```
aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagtgc tctcttgatc ctacaaacag 120
acattttcca ctcgtgtttc catagtgtgt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225
```

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaaatt ctgagggttg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
```

140

```

tcatcccat cccatgccaa aggaagaccc tccctccttg gtcacagcc ttctctaggc 180
ttccagtg ctcaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtg 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatccac ccct 334

```

```

<210> 406
<211> 216
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

```

```

<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216

```

```

<210> 407
<211> 413
<212> DNA
<213> Homo sapiens

```

```

<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc ctgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gacccagtg tcagattcta cacctggcca ctcagggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcatt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagtcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413

```

```

<210> 408
<211> 183
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(183)
<223> n = A,T,C or G

```

```

<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gtaaatcctt aaagggctan ntaatcctta actagtcctt ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttctggcta cccatgtact 180
ntt 183

```

```

<210> 409
<211> 250
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

141

&lt;222&gt; (1)...(250)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 409

```

cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gccccagga cagcgtgggc tatgtttaca gcgctcctt gctggggggg 240
ggcctatgc                                     250

```

&lt;210&gt; 410

&lt;211&gt; 306

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(306)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 410

```

ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tcccatattg aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccagggacc ttggaaacag ttggcactgt aagggtgctt ctccccaaga cacatcctaa 180
aagggtgtgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atcttttita aactggaaag ttcaattgng aaaatgaata 300
tcntgc                                     306

```

&lt;210&gt; 411

&lt;211&gt; 261

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(261)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 411

```

agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa gngaggcaa a                                     261

```

&lt;210&gt; 412

&lt;211&gt; 241

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(241)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 412

```

gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120

```

142

actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180  
 ctgggagatt tctctgggta cattgaattc ccaaactacc cangcaatta ccagccaac 240  
 a 241

<210> 413  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(231)  
 <223> n = A,T,C or G

<400> 413  
 aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60  
 ctcatccaag ttctctagtag ctctctcttg ttgtgaagga taatcaaact gaacaacaaa 120  
 aagtttactc tctctatttg gaacctaaaa actctcttct tcttgggtct gagggctcca 180  
 agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414  
 <211> 234  
 <212> DNA  
 <213> Homo sapiens

<400> 414  
 actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60  
 gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120  
 gtgagccaag gagggagggt ctctcttttg catgggatgg ggatgaagta aggagaggga 180  
 ctggaccccc tggaagctga ttactatgg ggggagggtg attgaagtcc tcca 234

<210> 415  
 <211> 217  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(217)  
 <223> n = A,T,C or G

<400> 415  
 gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60  
 caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120  
 cacctagcaa tagtagaatt cagtctact tctgaggcca gaagaatggg tcagaaaaat 180  
 antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416  
 <211> 213  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(213)  
 <223> n = A,T,C or G

<400> 416

143

```

atgcataatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtgggtaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag                                     213

```

<210> 417  
 <211> 303  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

```

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaata ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggccacacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt                                     303

```

<210> 418  
 <211> 328  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

```

<400> 418
tttttgccgg tgggtgggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcgcc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
tcagnngtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgtan gattacaggc cgtgagcc                                     328

```

<210> 419  
 <211> 389  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(389)  
 <223> n = A,T,C or G

```

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60
accctgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
cttgcttctt ctctgtggct ccattcatag cacagttgtt gcaactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaagt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtctt ctgctctatc agccatcacg 360

```

144

tggcagccac tcnggctgtg tcgacgcgg

389

&lt;210&gt; 420

&lt;211&gt; 408

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 420

```
gttcctccta actcctgcc aaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggtc tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgacttttgt gtttcggcat ggagaccgaa 180
gtcccatgga cacctttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgtatg acaaacctgg caagcccg 408
```

&lt;210&gt; 421

&lt;211&gt; 352

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (352)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 421

```
gctcaaaaat ctttttactg atnngcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttctctccc accacnatat acttgacgtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352
```

&lt;210&gt; 422

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 422

```
atgccaccat gctggcaatg cagcgggagg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcatagcaa ggtgccggcg atcgcgggcg cgtcaatcct ggccaaggtc agccgtgac 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcgggcgg cataagggct 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttcgg ccggtacggc tggcctatga aaattat 337
```

&lt;210&gt; 423

&lt;211&gt; 310

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (310)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 423

145

```

gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tcaactgacag aacagggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtcctgcc 300
tccgagtta                                     310

```

&lt;210&gt; 424

&lt;211&gt; 370

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(370).

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 424

```

gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
caactgacaga acagggtctt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacagggtga gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg                                     370

```

&lt;210&gt; 425

&lt;211&gt; 216

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(216)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 425

```

aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaataga 60
taacaacnca acatcaaggc aananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggntacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtntntg aggagg                                     216

```

&lt;210&gt; 426

&lt;211&gt; 596

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 426

```

cttcagtgga ggataaccct gttgcccggg gccgagggtc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgtaa 300
ttaaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattgggtc tactgcctga 540
gtcccgcgtg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct      596

```



146

<210> 427  
 <211> 107  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(107)  
 <223> n = A,T,C or G

<400> 427  
 gaagaattca agttagggtt attcaaaggg cttacngaga atcctanacc caggncaccag 60  
 cccgggagca gccttanaga gtcctgttt gactgcccgg ctcagng 107

<210> 428  
 <211> 38  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(38)  
 <223> n = A,T,C or G

<400> 428  
 gaacttcna anaangactt tattcactat ttacatt 38

<210> 429  
 <211> 544  
 <212> DNA  
 <213> Homo sapiens

<400> 429  
 ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60  
 attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120  
 atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180  
 tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240  
 gccttcact tcaattacac ctcaactacc atcctctcct gttggttctg tctgtcttca 300  
 agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360  
 tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420  
 gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480  
 acctcaaca gtttagagaga tatgcatac cagggatttt ttgccagggtg gtaggagaga 540  
 ttat 544

<210> 430  
 <211> 507  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(507)  
 <223> n = A,T,C or G

<400> 430  
 cttatcncaa tggggctccc aaacttggct gtgcagtga aactccgggg gaattttgaa 60  
 gaacactgac acccatcttc caccgccaca ctctgattta attgggctgc agtgagaaca 120

```

gagcatcaat ttaaaaagct gccagaatg ttntcctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgagga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagttaa tggataatct aatgtgcttc tagtaggcac agggctocca ggccaggcct 420
cattctctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507

```

```

<210> 431
<211> 392
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aacctatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct 392

```

```

<210> 432
<211> 387
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G

```

```

<400> 432
ggtatccnta cataatcaaa tatactgtga gtacatgttt tcattggngt agattaccac 60
aaatgaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgna gtccagccac tngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tatittgctt ctgtctgnga 240
attctgttgc ttctgggcca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt 387

```

```

<210> 433
<211> 281
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A,T,C or G

```

```

<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60

```

148

```

ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnagag ntctctgtnt gccactgtgt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

```

&lt;210&gt; 434

&lt;211&gt; 484

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 434

```

ttttaaaata agcatttagt gctcagtcco tactgagtac tctttctctc ccctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtaga tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaacat ttcaccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaacc 360
tgtccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484

```

&lt;210&gt; 435

&lt;211&gt; 424

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 435

```

gcgccgctca gagcaggta ctttctgcct tccacgtcct ccttcaagga agcccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatgggtc ggggtgacct 240
cttgagagga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424

```

&lt;210&gt; 436

&lt;211&gt; 667

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(667)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 436

```

accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattctct tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagttagat aggattccag atgtctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtaacagt ctgtgcttcg aatataaacc 360
tgttcagtgt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgtcccat gccagctggg gtgagttggc caaatccttg tggcatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcgggtctc atgccgaac 540
accaaagtca caaacttcaa ctcttgggt agtaacttc ggtctagcca gaaaaaagg 600
agaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660

```

149

tggtgag

667

&lt;210&gt; 437

&lt;211&gt; 693

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtaactct ctattttcac ccctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatggt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgagggtgt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgttg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc                                     693

```

&lt;210&gt; 438

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac ettctgactc 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctggttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

&lt;210&gt; 439

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

```

gttcctnnta actcctgcc aaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggtc tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgacttttgt gtttcggcat ggagaccgaa 180
gtccattga cacccttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcgcccgcg 420
aatttagtag t                                     431

```

&lt;210&gt; 440

&lt;211&gt; 523

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 440

```

agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcactcga tgagaacaag cta 523

```

&lt;210&gt; 441

&lt;211&gt; 430

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 441

```

gttctctcta actcctgcc aacacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtgtg tgactttggt gtttcggcat ggagaccgaa 180
gtccatttga cacccttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag 430

```

&lt;210&gt; 442

&lt;211&gt; 362

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 442

```

ctaaggaatt agtagtggtc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcttgtaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180
atgttttagaa atggtcattt tacggaaaaa ttgaaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaataaa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362

```

&lt;210&gt; 443

&lt;211&gt; 624

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(624)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 443

```

ttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtag tcagttagga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaatttg ccaactttct attaacttgg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaaaggga gttatgaggc ttaaatgaac 360

```

```

taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgcta 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtocctat ctgctaaaca gatc 624

```

```

<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

```

```

<400> 444
gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgggt gtcagcaa at ccttgaatgc 180
tgcttaatgt gagagggttg taaaatcctt tgtgcaacac tctaactccc tgaatgttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacacctg gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa ttagtagta 420
gtaga 425

```

```

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

```

```

<400> 445
catgtttatg nttttggatt actttgggca cctagtgttt ctaaactcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcattgtggc agattattgg atgtagtctt cttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtgtgtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta ttctctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcctctcc tcttgtatct tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtag 414

```

```

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G

```

```

<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120

```

152

```

atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaactttc caaccttcca ggaaatgcc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatggt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccctg catttggtgt 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g 631

```

<210> 447  
 <211> 585  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(585)  
 <223> n = A,T,C or G

```

<400> 447
ccttgggaaa antntcacia tataaagggt cgtagacttt actccaaatt ccaaaaaggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaaggtgt caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggcta gtacacttcg gtcta 585

```

<210> 448  
 <211> 93  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(93)  
 <223> n = A,T,C or G

```

<400> 448
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan ggccnccat 60
ggctccctag tgccctggag agganggggc tag 93

```

<210> 449  
 <211> 706  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(706)  
 <223> n = A,T,C or G

```

<400> 449
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60

```

153

```

ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtcccattc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct cttagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706

```

&lt;210&gt; 450

&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 450

```

gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
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aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaagg agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggg cgacgcggcc 480
gcgaatttag tag 493

```

&lt;210&gt; 451

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(501)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 451

```

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aacgccaggg ttttccagat cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300
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cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

```

&lt;210&gt; 452

&lt;211&gt; 51

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(51)

&lt;223&gt; n = A,T,C or G



154

<400> 452  
agacgggtttc accnttataa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453  
<211> 317  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(317)  
<223> n = A,T,C or G

<400> 453  
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ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180  
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
cccacaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
taccatgtc tttatta 317

<210> 454  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 454  
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agaagaccaa attcttctgc atcccagctt gcaaacaata ttgttcttct aggtctccac 180  
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 455  
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gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180  
caaagaattt ctcatagcac agctcacaat acagggtcctc tttctcctct a 231

<210> 456  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 456  
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tgcaactcaa ttcctttatc aggaataact acatagccac tatttataaa gccattggaa 180  
cctttttatt tgggtgcagct gctagtcagt cctgactga cattgccaag t 231

<210> 457  
<211> 231  
<212> DNA

155

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(231)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 457

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tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgect catttcctct gaggtgtcgc tggcttttgt g 231
```

&lt;210&gt; 458

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 458

```
aggtctgggt cccccactt ccactcccct ctactctctc taggactggg ctgggccaag 60
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acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtctctggg taggcatttt ggggggcccag accccaggag aagaagattc t 231
```

&lt;210&gt; 459

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 459

```
ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gccaccagt cctaaccgga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231
```

&lt;210&gt; 460

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 460

```
gcagggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcaccc tattcttggg ggtgcttct tcacagtgat catgaagcct agcagcaaat 120
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a 231
```

&lt;210&gt; 461

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 461

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gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgcctg tgtgtcctgg 120
gtgggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
aggggggattc catggcactg atagagccct atagtctcag agctgggaat t 231
```

&lt;210&gt; 462

156

<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 462  
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gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180  
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 463  
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catttgacag gtgtcttttc ctctggacct cgggtgtccc atctgagtga gaaaaggcag 180  
tggggagggt gatcttccag tcgaagcggg atagaagccc gtgtgaaaag c 231

<210> 464  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 464  
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cctgcttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
ggtgccagcg caccagctag atgctctgta acttctagc cccattttcc c 231

<210> 465  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 465  
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aggatggcac aatttttgct tgtgttcata atatactcag attagttcag ctccatcaga 180  
taaactggag acatgcagga cattagggtg gtgttgtagc tctggtaatg a 231

<210> 466  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 466  
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ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaaccat ttgccaggga 120  
cctgtgcaat caaatattgt ggagaattcc ctgactggag aagtcacaaa gactatagga 180  
aataatggag accagtccca caagatgaca accagtcgtt gtgtgcggct g 231

<210> 467  
<211> 311  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 467

```

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tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240
tgtgacctgc tgggcctccc aatagactaa caggcagtg cagttggacc caagagaaga 300
ctgcagcaga c                                     311

```

&lt;210&gt; 468

&lt;211&gt; 3112

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 468

```

catttgtgtg ggagaaaaac agaggggaga tttgtgtggc tgcagccgag ggagaccagg 60
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aaatgggata cacagtatga tctataaagt gggatatagt atgatctact tcactgggtt 420
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tttccattcc agttggcttc ttgggtttgc tagctgcac actagtcac tttaaataaat 720
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```

&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

```

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tatttctttc aattaactac aaggacaaac acatctcaaa gttgagataa gtgaccagta 120
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tttgactgac atgaattctg tgaagagctt gttggatatt gtgatagaga tagagaaatg 240
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aatggaatt 2229

```

&lt;210&gt; 470

&lt;211&gt; 2426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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gcatgaattc tgtgaaaagc ttgttgata ttgtgataga gatagagaaa tgaagtatat 240
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gggtgacggt tttgcccac acaatg 2426
```

&lt;210&gt; 471

&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

```
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aaatattaaa aatgagtgtg gctggatata tggagaatgt tgggccaga aggaaccgta 120
gagatcagat attacaacag ctttgtttt agggtagaa atatgaaatg atttggttat 180
gaacgcacag ttaggcagc agggccagaa tccctgacct ctgccccgtg gttatctcct 240
ccccagcttg gctgcctcat gtcacacag tattccattt tgtttgttgc atgtcttctg 300
aagccatcaa gatcttctc tctgttttcc tctcatttgt aatgctcact ttgtgacttc 360
atttcaaatc tgtaatcccg ttcaataaaa tatccacaac aggatctgtt ttccctgcca 420
```

160

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tcctttaagg aacacatcaa ttcattttct aatgtccttc cctcacaagc gggaccaggc 480
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gtgcttcctt ttgtgcttcc tgtgtgtgtg gatattttaa ggggctggaa atgtgcaaaa 600
acatgtcact acttagacat tatattgtca tcttgcgtgt tctagtgtat ttaattatct 660
ccatttcage agatgtgtgg cctcagatgg taaagtcagc agcctttctt atttctcacc 720
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cacaaatctc ccctctgttt ttctgatgcc ag 812

```

&lt;210&gt; 472

&lt;211&gt; 515

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(515)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 472

```

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gttccagaat tatttgctct tgagcccggt tgaatctcag caagaggaac caccaactga 180
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gaaaaaaaaa naaaaaaaaa aaanaaaaaa aaaaa 515

```

&lt;210&gt; 473

&lt;211&gt; 5829

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 473

```

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tgcaacagcc tgagtggctg ccacctgata gctgatggag cagaggcctg aggaaaatca 180
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162

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aaaaaaaaa 5829

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&lt;210&gt; 474

&lt;211&gt; 1594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

```

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&lt;210&gt; 475

&lt;211&gt; 2414

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (33)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 475

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aaaaaaaaaa aaaa 2414

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&lt;210&gt; 476

&lt;211&gt; 3434

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 476

```

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gccagtggta ccaccaggg gacttgtgct tctgtggccc aggccagacg tagaatttga 240
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aaaaaaaaa aaaa 3434

```

&lt;210&gt; 477

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

165

&lt;400&gt; 477

```

Met Asp Gly His Thr Asp Ile Trp Arg Asn His Met Asp Thr Pro Pro
      5                      10                      15
His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
      20                      25                      30
Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
      35                      40                      45
His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
      50                      55                      60
His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
      65                      70                      75                      80
Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
      85                      90                      95
Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
      100                     105                     110
Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
      115                     120                     125
Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
      130                     135                     140

```

&lt;210&gt; 478

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 478

```

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
      5                      10                      15
Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
      20                      25                      30
Gly Glu Ile Thr Trp Thr His His Thr Ile Thr Gly Thr Gln Thr
      35                      40                      45
His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
      50                      55                      60
Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
      65                      70                      75                      80
Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
      85                      90                      95
His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
      100                     105                     110
Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
      115                     120                     125
His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
      130                     135                     140

```

&lt;210&gt; 479

&lt;211&gt; 222

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 479

```

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
      5                      10                      15
Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
      20                      25                      30

```

166

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr  
           35                  40                  45  
 His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr  
           50                  55                  60  
 Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr  
           65                  70                  75                  80  
 Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser  
                   85                  90                  95  
 His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val  
                   100                  105                  110  
 Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val  
           115                  120                  125  
 Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr  
           130                  135                  140  
 Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His  
           145                  150                  155                  160  
 Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala  
                   165                  170                  175  
 Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp  
                   180                  185                  190  
 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala  
           195                  200                  205  
 Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val  
           210                  215                  220

&lt;210&gt; 480

&lt;211&gt; 144

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 480

Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val  
                   5                  10                  15  
 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr  
                   20                  25                  30  
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg  
                   35                  40                  45  
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly  
           50                  55                  60  
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln  
           65                  70                  75                  80  
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys  
                   85                  90                  95  
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly  
                   100                  105                  110  
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu  
           115                  120                  125  
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly  
           130                  135                  140

&lt;210&gt; 481

&lt;211&gt; 167

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 481

167

```

Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
      5              10              15
Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
      20              25              30
Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
      35              40              45
Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
      50              55              60
Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro
      65              70              75              80
Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg
      85              90              95
Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala
      100             105             110
Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His
      115             120             125
Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe
      130             135             140
Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser
      145             150             155             160
Trp Leu Ser Arg Gly Arg Pro
      165

```

<210> 482  
 <211> 143  
 <212> PRT  
 <213> Homo sapiens

```

<400> 482
Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val
      5              10              15
Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu
      20              25              30
Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg
      35              40              45
Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly
      50              55              60
Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe
      65              70              75              80
Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr
      85              90              95
Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly
      100             105             110
Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys
      115             120             125
Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly
      130             135             140

```

<210> 483  
 <211> 143  
 <212> PRT  
 <213> Homo sapiens

```

<400> 483
Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5              10              15
Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala

```

168

```

      20      25      30
Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35      40      45
Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50      55      60
Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65      70      75      80
Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85      90      95
Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100      105      110
Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115      120      125
Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130      135      140

```

<210> 484  
 <211> 30  
 <212> PRT  
 <213> Homo Sapien

```

      <400> 484
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1          5          10          15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20          25          30

```

<210> 485  
 <211> 31  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

```

      <400> 485
gggaagctta tcacctatgt gccgcctctg c

```

31

<210> 486  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

```

      <400> 486
gcgaattctc acgctgagta tttaggcc

```

27

<210> 487  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 487

169

cccgattct tagctgccca tccgaacgcc ttcac

36

<210> 488  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 488  
 gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489  
 <211> 19  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 489  
 Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
 1 5 10 15  
 Ser Val Ala

<210> 490  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 490  
 Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys  
 1 5 10 15  
 Leu Ser His Ser  
 20

<210> 491  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 491  
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu  
 1 5 10 15  
 Thr Gly Phe Thr  
 20

<210> 492  
 <211> 20  
 <212> PRT



170

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
			20												

&lt;210&gt; 493

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
			20												

&lt;210&gt; 494

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
			20												

&lt;210&gt; 495

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 495

Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu	Pro	Gly	Pro	Lys	Pro	Gly	Ala	Pro
1				5					10					15	
Phe	Pro	Asn	Gly												
			20												

&lt;210&gt; 496

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

171

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 496

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 497

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 497

Leu	Leu	Pro	Pro	Pro	Pro	Ala	Leu	Cys	Gly	Ala	Ser	Ala	Cys	Asp	Val
1				5				10						15	
Ser	Val	Arg	Val												
			20												

&lt;210&gt; 498

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 498

Asp	Val	Ser	Val	Arg	Val	Val	Val	Gly	Glu	Pro	Thr	Glu	Ala	Arg	Val
1				5				10						15	
Val	Pro	Gly	Arg												
			20												

&lt;210&gt; 499

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1				5				10						15	
Ser	Ala	Phe	Leu												
			20												

&lt;210&gt; 500

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

172

&lt;223&gt; Made in a lab

&lt;400&gt; 500

Leu	Asp	Ser	Ala	Phe	Leu	Leu	Ser	Gln	Val	Ala	Pro	Ser	Leu	Phe	Met
1				5					10					15	
Gly	Ser	Ile	Val												
			20												

&lt;210&gt; 501

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 501

Phe	Met	Gly	Ser	Ile	Val	Gln	Leu	Ser	Gln	Ser	Val	Thr	Ala	Tyr	Met
1				5					10					15	
Val	Ser	Ala	Ala												
			20												

&lt;210&gt; 502

&lt;211&gt; 414

&lt;212&gt; DNA

&lt;213&gt; Homo Sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(414)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 502

caccatggag	acaggcctgc	gctggctttt	cctggctcgt	gtgctcaaag	gtgtccaatg	60
tcagtcggtg	gaggagtccg	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgtagagtt	tttggaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
aggggaaggg	ctggaatgga	tcggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnat	ccaaaacctn	gaccacgggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatTTTTg	tggcagaatg	aatactggta	atagtgggtg	360
gaagaatatt	tggggccca	gcaccctggt	caccgtntcc	tcagggcaac	ctaa	414

&lt;210&gt; 503

&lt;211&gt; 379

&lt;212&gt; DNA

&lt;213&gt; Homo Sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(379)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 503

atnccatggt	gcttgggtcaa	aggtgtccag	tgctcagtcg	tggaggagtc	cgggggtcgc	60
ctgggtcacgc	ctgggacacc	cctgacactc	acctgcaccc	tntctggatt	ngacatcagt	120
agctatggag	tgagctgggt	ccgccaggct	ccagggaagg	ggctggnata	catcggtatca	180
ttagtagtag	tggtagattt	tacgcgagct	gggcgaaagg	ccgattcacc	atttccaaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	aggggggttt	aattataaag	acatttgggg	cccaggcacc	ctggtcaccg	360

173

tntccttagg gcaacctaa

379

<210> 504  
 <211> 19  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 504  
 Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu  
 1 5 10 15  
 Asn Ser Ala

<210> 505  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 505  
 Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr  
 1 5 10 15  
 Asn Thr Ala Asn  
 20

<210> 506  
 <211> 407  
 <212> DNA  
 <213> Homo Sapien

<400> 506  
 atggagacag gcctgcgctg gcttctctg gtcgctgccc tcaaagggtg ccagtgtcag 60  
 tcgctggagg agtccggggg tcgcttggtc acgcctggga caccctgac actcacctgc 120  
 accgtctctg gattctccct cagtagcaat gcaatgatct gggcccgcca ggctccaggg 180  
 aaggggctgg aatacatcgg atacattagt tatggtggta gcgcatacta cgcgagctgg 240  
 gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt 300  
 ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg 360  
 ttgtggggcc caggcaccct ggtcacccgc tcctcagggc aacctaa 407

<210> 507  
 <211> 422  
 <212> DNA  
 <213> Homo Sapien

<400> 507  
 atggagacag gcctgcgctg gcttctctg gtcgctgtgc tcaaagggtg ccagtgtcag 60  
 tcgctggagg agtccggggg tcgcttggtc acgcctggga caccctgac actcacctgt 120  
 acagtctctg gattctccct cagcaactac gacctgaact gggcccgcca ggctccaggg 180  
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cgcgaactgg 240  
 gcaaaaggcc ggttcacat ctccaaaacc tcgaccacgg tggatctcaa gatcgccagt 300  
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360  
 ggtccgtgct tgcgcatctg gggcccaggc accctgggtc cagtctcctt agggcaacct 420

174

aa

422

<210> 508  
 <211> 411  
 <212> DNA  
 <213> Homo Sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(411)  
 <223> n=A,T,C or G

<400> 508  
 atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaaggtgtc cagtgtcagt 60  
 cggtggagga gtccgggggt cgcttggtca cgctgggac acccctgaca ctcacctgca 120  
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180  
 aggggctgga atggatcgga atcattggta ctctggtga cacatactac gcgagggtgg 240  
 cgaaaggccg attcaccatc tcaaaaacct cgaccacggt gcatntgaaa atcnccagtc 300  
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360  
 ctggttatta taaaatctgg ggcccaggca ccctggtcac cgtctccttg g 411

<210> 509  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 509  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 510  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 510  
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile  
 1 5 10 15

<210> 511  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 511  
 Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys  
 1 5 10 15

175

<210> 512  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 512

Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu
1				5					10					15

<210> 513  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 513

Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Asx	Val	Tyr	Thr	Asn	Leu
1				5					10					15

<210> 514  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 514

Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser
1				5					10					15

<210> 515  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 515

Met	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg
1				5					10					15

<210> 516  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 516

Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

176

1                    5                    10                    15  
 <210> 517  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Made in a lab  
  
 <400> 517  
 Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met  
 1                    5                    10                    15  
  
 <210> 518  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Made in a lab  
  
 <400> 518  
 Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 1                    5                    10                    15  
  
 <210> 519  
 <211> 17  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Made in a lab  
  
 <400> 519  
 Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys  
 1                    5                    10                    15  
 Gly  
  
 <210> 520  
 <211> 25  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Made in a lab  
  
 <400> 520  
 Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr  
 1                    5                    10                    15  
 Glu Ala Arg Arg His Tyr Asp Glu Gly  
 20                    25  
  
 <210> 521  
 <211> 21  
 <212> PRT  
 <213> Artificial Sequence

177

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 522

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
			20												

&lt;210&gt; 523

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)... (254)

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10						15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
		20					25					30			
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
		35				40					45				
Val	Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln
	50				55					60					
Trp	Val	Leu	Ser	Ala	Thr	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly
65					70				75					80	
Leu	Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met
			85					90						95	
Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu
		100					105						110		
Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu
		115					120					125			
Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala
	130					135					140				
Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg
145					150					155					160



178

Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
 165 170 175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
 180 185 190  
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly  
 195 200 205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
 210 215 220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225 230 235 240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 245 250

<210> 524  
 <211> 765  
 <212> DNA  
 <213> Homo sapien

<400> 524  
 atggccacag caggaaatcc ctggggctgg ttcttggggg acctcatcct tgggtgtcgca 60  
 ggatcgctcg tctctggtag ctgcagccaa atcataaacg gcgaggactg cagcccgcac 120  
 tcgcagccct ggcaggcggc actgggtcatg gaaaaagaaat tggttctgctc gggcgctcctg 180  
 gtgcacccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240  
 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300  
 ctctccgtac ggcacccaga gtacaacaga cccttgcctc ctaacgacct catgctcctc 360  
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 420  
 tgccctaccg cggggaactc ttgcctcgtt tctggctggg gtctgctggc gaacggcaga 480  
 atgcctaccg tgctgcagtg cgtgaacgtg tcggtgggtg ctgaggagggt ctgcagtaag 540  
 ctctatgacc cgctgtacca cccagcatg ttctgcgccg gcggagggca agaccagaag 600  
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 660  
 gtgtcttttg gaaaagcccc gtgtggccaa gttggcgtgc caggtgtota caccaacctc 720  
 tgcaaatcca ctgagtggat agagaaaacc gtccaggcca gttaa 765

<210> 525  
 <211> 254  
 <212> PRT  
 <213> Homo sapien

<400> 525  
 Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile  
 1 5 10 15  
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile  
 20 25 30  
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu  
 35 40 45  
 Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln  
 50 55 60  
 Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly  
 65 70 75 80  
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
 85 90 95  
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu  
 100 105 110  
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu  
 115 120 125  
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala  
 130 135 140  
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg

179

145		150		155		160
Met Pro Thr Val	Leu Gln Cys Val	Asn Val Ser Val	Val Ser Glu Glu			
	165	170	175			
Val Cys Ser Lys	Leu Tyr Asp Pro	Leu Tyr His Pro	Ser Met Phe Cys			
	180	185	190			
Ala Gly Gly Gly	Gln Asp Gln Lys	Asp Ser Cys Asn	Gly Asp Ser Gly			
	195	200	205			
Gly Pro Leu Ile	Cys Asn Gly Tyr	Leu Gln Gly Leu	Val Ser Phe Gly			
	210	215	220			
Lys Ala Pro Cys	Gly Gln Val Gly	Val Pro Gly Val	Tyr Thr Asn Leu			
	225	230	235			240
Cys Lys Phe Thr	Glu Trp Ile Glu	Lys Thr Val Gln	Ala Ser			
	245	250				

&lt;210&gt; 526

&lt;211&gt; 963

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 526

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atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60
aaagcccatt tctgggttgg cttcccctc ctttccatgt atgtagtggc aatgtttgga 120
aactgcatcg tgggtcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttctctgca tgcttgcagc cattgacctg gccttatcca catccaccat gcctaagatc 240
cttgcccttt tctggtttga ttcccagag attagtcttg aggcctgtct taccagatg 300
ttctttattc atgccctctc agccattgaa tccaccatcc tgctggccat ggcctttgac 360
cgttatgtgg ccatctgcca cccactgcgc catgctgcag tgctcaacaa tacagtaaca 420
gccagattg gcatcggtggc tgtggtccgc ggatccctct tttttttccc actgcctctg 480
ctgatcaagc ggctggcctt ctgccactcc aatgtcctct cgcaactccta ttgtgtccac 540
caggatgtaa tgaagtggc ctatgcagac actttgccca atgtggtata tgggtcttact 600
gccattctgc tggatcatggg cgtggacgta atgttcatct ccttgtccta ttttctgata 660
atacgaacgg ttctgcaact gccttccaag tcagagcggg ccaaggcctt tggaaacctgt 720
gtgtcacaca ttggtgtggt actgccttc tatgtgccac ttattggcct ctcaagtgtg 780
caccgctttg gaaacagcct tcatcccat gtgcgtgttg tcatgggtga catctacctg 840
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cgggtgctgg ctatgttcaa gatcagctgt gacaaggact tgcaggctgt gggaggcaag 960
tga
963

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&lt;210&gt; 527

&lt;211&gt; 320

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 527

Met Ser Ser Cys	Asn Phe Thr His	Ala Thr Phe Val	Leu Ile Gly Ile
	5	10	15
Pro Gly Leu Glu	Lys Ala His Phe	Trp Val Gly Phe	Pro Leu Leu Ser
	20	25	30
Met Tyr Val Val	Ala Met Phe Gly	Asn Cys Ile Val	Val Phe Ile Val
	35	40	45
Arg Thr Glu Arg	Ser Leu His Ala	Pro Met Tyr Leu	Phe Leu Cys Met
	50	55	60
Leu Ala Ala Ile	Asp Leu Ala Leu	Ser Thr Ser Thr	Met Pro Lys Ile
	65	70	75
Leu Ala Leu Phe	Trp Phe Asp Ser	Arg Glu Ile Ser	Phe Glu Ala Cys
	85	90	95
Leu Thr Gln Met	Phe Phe Ile His	Ala Leu Ser Ala	Ile Glu Ser Thr
	100	105	110

180

Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro  
 115 120 125  
 Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly  
 130 135 140  
 Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu  
 145 150 155 160  
 Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser  
 165 170 175  
 Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu  
 180 185 190  
 Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val  
 195 200 205  
 Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val  
 210 215 220  
 Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys  
 225 230 235 240  
 Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly  
 245 250 255  
 Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg  
 260 265 270  
 Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro  
 275 280 285  
 Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala  
 290 295 300  
 Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys  
 305 310 315 320

<210> 528  
 <211> 20  
 <212> DNA  
 <213> Homo Sapien

<400> 528  
 actatggtcc agaggctgtg

20

<210> 529  
 <211> 20  
 <212> DNA  
 <213> Homo Sapien

<400> 529  
 atcacctatg tgccgcctct

20

<210> 530  
 <211> 1852  
 <212> DNA  
 <213> Homo sapiens

<400> 530  
 ggcacgagaa ttaaaaccct cagcaaaaca ggcatagaag ggacatacct taaagtaata 60  
 aaaaccacct atgacaagcc cacagccaac ataatactaa atgggggaaaa gttagaagca 120  
 tttcctctga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc 180  
 tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240  
 ttattgactt gcctgtgtta gaccggaaga gctgggggtgt ttctcaggag ccaccgtgtg 300  
 ctgcggcagc ttcgggataa cttgaggctg catcactggg gaagaaacac aytctgtgcc 360  
 gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg 420  
 ggagttcttc cttcatagtt catccatagtg gctccagagg aaaattatat tattttgtta 480  
 tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgaatgtgtga 540

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ttgggtaggt tccaccatgt tgccgcagat gacatgattt cagtacctgt gtctggctga 600
aaagtgtttt tttgtgaatg gatattgtgg tttctggatc tcatcctctg tgggtggaca 660
gctttctcca ccttgctgga agtgacctgc tgtccagaag tttgatggct gaggagtata 720
ccatcgtgca tgcattcttc atttctctgca tttcttctc cctggatgga cagggggagc 780
ggcaagagca acgtgggcac ttctggagac cacaacgact cctctgtgaa gacgcttggg 840
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aacgtgggtc cttggggaga ctacgatgac agcgcttca tggatcccag gtaccacgtc 960
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gatctcatcg tcatgctcag ggacacggat gtgaacaaga gggacaagca aaaggaggact 1080
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gatgaagtat gaaataccac tctacactat gctgtctaca atgaagataa attaatggcc 1320
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aagacttaaa gctgacatca gaggaagagt cacaaaggct taaaggaagt gaaaacagcc 1740
agccagagct agaagattta tgctattga agaagaatga agaacacgga agtactcatg 1800
tgggattccc agaaaacctg actaacggtg ccgctgctgg caatggtgat ga 1852

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&lt;210&gt; 531

&lt;211&gt; 879

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 531

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atgcattctt catttctctgc atttcttctt ccctggatgg acagggggag cggaagagc 60
aacgtgggca cttctggaga ccacaacgac tcctctgtga agacgcttgg gagcaagagg 120
tgcaagtggg gctgccactg cttcccctgc tgcaggggga gcggcaagag caacgtggtc 180
gcttggggag actacgatga cagcgcttgc atggatccca ggtaccacgt ccatggagaa 240
gatctggaca agctccacag agctgcctgg tggggtaaag tcccagaaa ggatctctac 300
gtcatgctca gggacacgga tgtgaacaag agggacaagc aaaaggaggac tgctctacat 360
ctggcctctg ccaatgggaa ttcagaagta gtaaaactcg tgctggacag acgatgtcaa 420
cttaatgtcc ttgacaacaa aaaggaggaca gctctgacaa aggccgtaca atgccaggaa 480
gatgaatgtg cgtaaatgtt gctggaacat ggcactgatc caaatattcc agatgagtat 540
ggaaatacca ctctacacta tgctgtctac aatgaagata aattaatggc caaagcactg 600
ctcttatacg gtgctgatat cgaatcaaaa aacaagcatg gcctcacacc actgctactt 660
ggtatacatg agcaaaaaca gcaagtgggt aaatttttaa tcaagaaaaa agcgaattta 720
aatgcgtggt atagatatgg aagaactgct ctcatacttg ctgtatgttg tggatcagca 780
agtatagtca gccctctact tgagcaaaat gttgatgtat cttctcaaga tctggaaaga 840
cggccagaga gtatgctgtt tctagtcatc atcatgtaa 879

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&lt;210&gt; 532

&lt;211&gt; 292

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 532

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Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly
      5              10              15
Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser
      20              25              30
Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
      35              40              45
Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp

```

182

50 55 60  
 Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu  
 65 70 75 80  
 Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg  
 85 90 95  
 Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp  
 100 105 110  
 Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser  
 115 120 125  
 Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu  
 130 135 140  
 Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu  
 145 150 155 160  
 Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile  
 165 170 175  
 Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu  
 180 185 190  
 Asp Lys Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile Glu  
 195 200 205  
 Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu  
 210 215 220  
 Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu  
 225 230 235 240  
 Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys  
 245 250 255  
 Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp  
 260 265 270  
 Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu  
 275 280 285  
 Val Ile Ile Met  
 290

<210> 533  
 <211> 801  
 <212> DNA  
 <213> Homo sapiens

<400> 533  
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 tatgccactg cagcattctt gggtgccaag aggccaaacca caggccatct tgagaaggag 180  
 ttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240  
 ccctggccag acatagaatt tgtgccaagg caggacaagc tcaactcagag cagcgtgtta 300  
 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360  
 tctgcagggg tgcgtctgga ggaggtggac cagccaccaa ccttaccag tcaaggaagt 420  
 ggatggccat gttccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480  
 ttaggaaaag cagatggccc ttggccctac ctttttgtta gaagaactga tgttccatgt 540  
 cctgcagcga gtgaggttgg tggctgtgcc cccagctcct ggcacaccct cgcagaggtg 600  
 actggttgct ctttgagccc tcttagcctt gccagcatg cacaagcctc agtgctacta 660  
 ctgtgctaca aatggagcca tataggggaa acgagcagcc atctcaggag caaggtgtat 720  
 gctgcctttg ggggctccag tccttgcctc aagggtctta tgtcactgtg ggcttcttgg 780  
 ttgccaagag gcagaccata g 801

<210> 534  
 <211> 266  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 534

Met Tyr Lys Leu Gln Cys Asn Asn Cys Ala Thr Asn Gly Ala Thr Glu  
                   5                  10                  15  
 Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala  
           20                  25                  30  
 Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val  
           35                  40                  45  
 Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His  
           50                  55                  60  
 Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp  
           65                  70                  75                  80  
 Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln  
                   85                  90                  95  
 Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn  
                   100                  105                  110  
 Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu  
           115                  120                  125  
 Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys  
           130                  135                  140  
 Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala  
           145                  150                  155                  160  
 Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr  
                   165                  170                  175  
 Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser  
           180                  185                  190  
 Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu  
           195                  200                  205  
 Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Cys Tyr Lys  
           210                  215                  220  
 Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr  
           225                  230                  235                  240  
 Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu  
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&lt;210&gt; 535

&lt;211&gt; 6082

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 535

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&lt;211&gt; 6140

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&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;400&gt; 536

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&lt;210&gt; 537

&lt;211&gt; 1228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 537

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      20              25              30
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      35              40              45
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      50              55              60
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      65              70              75              80
Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser Tyr Leu Val Leu Gly
      85              90              95
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Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser
      115             120             125
Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys
      130             135             140
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln
      145             150             155             160
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg
      165             170             175

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188

Lys	Ala	Leu	Arg	Leu	Ser	Asn	Met	Ala	Met	Gly	Lys	Thr	Thr	Thr	Gly
		180						185						190	
Gln	Ile	Val	Asn	Leu	Leu	Ser	Asn	Asp	Val	Asn	Lys	Phe	Asp	Gln	Val
		195					200					205			
Thr	Val	Phe	Leu	His	Phe	Leu	Trp	Ala	Gly	Pro	Leu	Gln	Ala	Ile	Ala
	210					215				220					
Val	Thr	Ala	Leu	Leu	Trp	Met	Glu	Ile	Gly	Ile	Ser	Cys	Leu	Ala	Gly
225					230					235					240
Met	Ala	Val	Leu	Ile	Ile	Leu	Leu	Pro	Leu	Gln	Ser	Cys	Phe	Gly	Lys
			245						250					255	
Leu	Phe	Ser	Ser	Leu	Arg	Ser	Lys	Thr	Ala	Thr	Phe	Thr	Asp	Ala	Arg
		260						265					270		
Ile	Arg	Thr	Met	Asn	Glu	Val	Ile	Thr	Gly	Ile	Arg	Ile	Ile	Lys	Met
	275						280					285			
Tyr	Ala	Trp	Glu	Lys	Ser	Phe	Ser	Asn	Leu	Ile	Thr	Asn	Leu	Arg	Lys
	290					295					300				
Lys	Glu	Ile	Ser	Lys	Ile	Leu	Arg	Ser	Ser	Cys	Leu	Arg	Gly	Met	Asn
305					310					315					320
Leu	Ala	Ser	Phe	Phe	Ser	Ala	Ser	Lys	Ile	Ile	Val	Phe	Val	Thr	Phe
			325						330					335	
Thr	Thr	Tyr	Val	Leu	Leu	Gly	Ser	Val	Ile	Thr	Ala	Ser	Arg	Val	Phe
		340						345					350		
Val	Ala	Val	Thr	Leu	Tyr	Gly	Ala	Val	Arg	Leu	Thr	Val	Thr	Leu	Phe
		355					360					365			
Phe	Pro	Ser	Ala	Ile	Glu	Arg	Val	Ser	Glu	Ala	Ile	Val	Ser	Ile	Arg
	370					375					380				
Arg	Ile	Gln	Thr	Phe	Leu	Leu	Leu	Asp	Glu	Ile	Ser	Gln	Arg	Asn	Arg
385					390					395					400
Gln	Leu	Pro	Ser	Asp	Gly	Lys	Lys	Met	Val	His	Val	Gln	Asp	Phe	Thr
			405						410					415	
Ala	Phe	Trp	Asp	Lys	Ala	Ser	Glu	Thr	Pro	Thr	Leu	Gln	Gly	Leu	Ser
		420					425						430		
Phe	Thr	Val	Arg	Pro	Gly	Glu	Leu	Leu	Ala	Val	Val	Gly	Pro	Val	Gly
		435					440					445			
Ala	Gly	Lys	Ser	Ser	Leu	Leu	Ser	Ala	Val	Leu	Gly	Glu	Leu	Ala	Pro
	450					455					460				
Ser	His	Gly	Leu	Val	Ser	Val	His	Gly	Arg	Ile	Ala	Tyr	Val	Ser	Gln
465					470					475					480
Gln	Pro	Trp	Val	Phe	Ser	Gly	Thr	Leu	Arg	Ser	Asn	Ile	Leu	Phe	Gly
			485						490					495	
Lys	Lys	Tyr	Glu	Lys	Glu	Arg	Tyr	Glu	Lys	Val	Ile	Lys	Ala	Cys	Ala
		500						505					510		
Leu	Lys	Lys	Asp	Leu	Gln	Leu	Leu	Glu	Asp	Gly	Asp	Leu	Thr	Val	Ile
		515					520					525			
Gly	Asp	Arg	Gly	Thr	Thr	Leu	Ser	Gly	Gly	Gln	Lys	Ala	Arg	Val	Asn
	530					535					540				
Leu	Ala	Arg	Ala	Val	Tyr	Gln	Asp	Ala	Asp	Ile	Tyr	Leu	Leu	Asp	Asp
545					550					555					560
Pro	Leu	Ser	Ala	Val	Asp	Ala	Glu	Val	Ser	Arg	His	Leu	Phe	Glu	Leu
			565						570					575	
Cys	Ile	Cys	Gln	Ile	Leu	His	Glu	Lys	Ile	Thr	Ile	Leu	Val	Thr	His
			580					585					590		
Gln	Leu	Gln	Tyr	Leu	Lys	Ala	Ala	Ser	Gln	Ile	Leu	Ile	Leu	Lys	Asp
		595					600					605			
Gly	Lys	Met	Val	Gln	Lys	Gly	Thr	Tyr	Thr	Glu	Phe	Leu	Lys	Ser	Gly
	610					615					620				
Ile	Asp	Phe	Gly	Ser	Leu	Leu	Lys	Lys	Asp	Asn	Glu	Glu	Ser	Glu	Gln
625					630					635					640

Pro	Pro	Val	Pro	Gly	Thr	Pro	Thr	Leu	Arg	Asn	Arg	Thr	Phe	Ser	Glu
				645					650					655	
Ser	Ser	Val	Trp	Ser	Gln	Gln	Ser	Ser	Arg	Pro	Ser	Leu	Lys	Asp	Gly
		660						665					670		
Ala	Leu	Glu	Ser	Gln	Asp	Thr	Glu	Asn	Val	Pro	Val	Thr	Leu	Ser	Glu
		675					680					685			
Glu	Asn	Arg	Ser	Glu	Gly	Lys	Val	Gly	Phe	Gln	Ala	Tyr	Lys	Asn	Tyr
	690					695				700					
Phe	Arg	Ala	Gly	Ala	His	Trp	Ile	Val	Phe	Ile	Phe	Leu	Ile	Leu	Leu
705					710					715					720
Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln	Asp	Trp	Trp	Leu	Ser
				725					730					735	
Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val	Thr	Val	Asn	Gly	Gly
		740						745					750		
Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp	Tyr	Leu	Gly	Ile	Tyr
		755					760					765			
Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly	Ile	Ala	Arg	Ser	Leu
	770					775					780				
Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln	Thr	Leu	His	Asn	Lys
785					790					795					800
Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	Phe	Phe	Asp	Arg	Asn
				805					810					815	
Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	Asp	Ile	Gly	His	Leu
				820				825						830	
Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	Ile	Gln	Thr	Leu	Leu
		835					840					845			
Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	Val	Ile	Pro	Trp	Ile
	850					855					860				
Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	Ile	Phe	Leu	Arg	Arg
865					870					875					880
Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	Leu	Glu	Ser	Thr	Thr
				885					890					895	
Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	Leu	Gln	Gly	Leu	Trp
			900					905						910	
Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	Gln	Glu	Leu	Phe	Asp
		915					920					925			
Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	Leu	Phe	Leu	Thr	Thr
		930				935					940				
Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	Cys	Ala	Met	Phe	Val
945					950					955					960
Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	Lys	Thr	Leu	Asp	Ala
				965					970					975	
Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	Thr	Leu	Met	Gly	Met
		980						985					990		
Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	Glu	Asn	Met	Met	Ile
		995					1000					1005			
Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	Glu	Lys	Glu	Ala	Pro
		1010				1015					1020				
Trp	Glu	Tyr	Gln	Lys	Arg	Pro	Pro	Pro	Ala	Trp	Pro	His	Glu	Gly	Val
1025					1030					1035					1040
Ile	Ile	Phe	Asp	Asn	Val	Asn	Phe	Met	Tyr	Ser	Pro	Gly	Gly	Pro	Leu
				1045					1050					1055	
Val	Leu	Lys	His	Leu	Thr	Ala	Leu	Ile	Lys	Ser	Gln	Glu	Lys	Val	Gly
				1060				1065					1070		
Ile	Val	Gly	Arg	Thr	Gly	Ala	Gly	Lys	Ser	Ser	Leu	Ile	Ser	Ala	Leu
		1075					1080					1085			
Phe	Arg	Leu	Ser	Glu	Pro	Glu	Gly	Lys	Ile	Trp	Ile	Asp	Lys	Ile	Leu
		1090				1095						1100			

190

Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile  
 1105 1110 1115 1120  
 Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp  
 1125 1130 1135  
 Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu  
 1140 1145 1150  
 Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr  
 1155 1160 1165  
 Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu  
 1170 1175 1180  
 Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile  
 1185 1190 1195 1200  
 Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln  
 1205 1210 1215  
 Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys  
 1220 1225

&lt;210&gt; 538

&lt;211&gt; 1261

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 538

Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu  
 5 10 15  
 Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala  
 20 25 30  
 Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser  
 35 40 45  
 Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val  
 50 55 60  
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr  
 65 70 75 80  
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr  
 85 90 95  
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr  
 100 105 110  
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys  
 115 120 125  
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly  
 130 135 140  
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn  
 145 150 155 160  
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro  
 165 170 175  
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile  
 180 185 190  
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln  
 195 200 205  
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr  
 210 215 220  
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile  
 225 230 235 240  
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile  
 245 250 255  
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys  
 260 265 270  
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile

275	280	285
Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr		
290	295	300
Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu		
305	310	315
Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala		
	325	330
Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile		
	340	345
Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His		
	355	360
Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr		
	370	375
Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val		
385	390	395
Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu		
	405	410
Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile		
	420	425
Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser		
	435	440
Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val		
	450	455
Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly		
465	470	475
Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln		
	485	490
Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile		
	500	505
Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg		
	515	520
His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr		
	530	535
Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile		
545	550	555
Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu		
	565	570
Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn		
	580	585
Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn		
	595	600
Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro		
	610	615
Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro		
625	630	635
Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln		
	645	650
Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile		
	660	665
Phe Leu Ile Leu Leu Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln		
	675	680
Asp Trp Trp Leu Ser Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val		
	690	695
Thr Val Asn Gly Gly Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp		
705	710	715
Tyr Leu Gly Ile Tyr Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly		
	725	730
Ile Ala Arg Ser Leu Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln		
	735	

			740					745				750			
Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu
		755					760					765			
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys
		770					775					780			
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe
785					790					795				800	
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala
			805						810					815	
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe
			820					825					830		
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg
		835					840					845			
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser
		850				855					860				
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys
865					870					875					880
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe
			885						890					895	
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile
			900					905					910		
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala
		915					920					925			
-Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu
930						935					940				
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val
945					950					955					960
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu
			965						970					975	
Glu	Lys	Glu	Ala	Pro	Trp	Glu	Tyr	Gln	Lys	Arg	Pro	Pro	Pro	Ala	Trp
			980					985					990		
Pro	His	Glu	Gly	Val	Ile	Ile	Phe	Asp	Asn	Val	Asn	Phe	Met	Tyr	Ser
		995					1000					1005			
Pro	Gly	Pro	Leu	Val	Leu	Lys	His	Leu	Thr	Ala	Leu	Ile	Lys	Ser	
		1010				1015					1020				
Gln	Glu	Lys	Val	Gly	Ile	Val	Gly	Arg	Thr	Gly	Ala	Gly	Lys	Ser	Ser
1025					1030					1035					1040
Leu	Ile	Ser	Ala	Leu	Phe	Arg	Leu	Ser	Glu	Pro	Glu	Gly	Lys	Ile	Trp
				1045					1050					1055	
Ile	Asp	Lys	Ile	Leu	Thr	Thr	Glu	Ile	Gly	Leu	His	Asp	Leu	Arg	Lys
			1060					1065					1070		
Lys	Met	Ser	Ile	Ile	Pro	Gln	Glu	Pro	Val	Leu	Phe	Thr	Gly	Thr	Met
		1075					1080					1085			
Arg	Lys	Asn	Leu	Asp	Pro	Phe	Asn	Glu	His	Thr	Asp	Glu	Glu	Leu	Trp
		1090				1095					1100				
Asn	Ala	Leu	Gln	Glu	Val	Gln	Leu	Lys	Glu	Thr	Ile	Glu	Asp	Leu	Pro
1105					1110					1115					1120
Gly	Lys	Met	Asp	Thr	Glu	Leu	Ala	Glu	Ser	Gly	Ser	Asn	Phe	Ser	Val
			1125						1130					1135	
Gly	Gln	Arg	Gln	Leu	Val	Cys	Leu	Ala	Arg	Ala	Ile	Leu	Arg	Lys	Asn
			1140				1145					1150			
Gln	Ile	Leu	Ile	Ile	Asp	Glu	Ala	Thr	Ala	Asn	Val	Asp	Pro	Arg	Thr
		1155					1160					1165			
Asp	Glu	Leu	Ile	Gln	Lys	Lys	Ile	Arg	Glu	Lys	Phe	Ala	His	Cys	Thr
		1170				1175					1180				
Val	Leu	Thr	Ile	Ala	His	Arg	Leu	Asn	Thr	Ile	Ile	Asp	Ser	Asp	Lys
1185					1190					1195					1200
Ile	Met	Val	Leu	Asp	Ser	Gly	Arg	Leu	Lys	Glu	Tyr	Asp	Glu	Pro	Tyr

193

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          1205          1210          1215
Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln
          1220          1225          1230
Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg
          1235          1240          1245
Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
          1250          1255          1260

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 <211> 10  
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 <213> Artificial Sequence

<220>  
 <223> Made in a lab

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<210> 540  
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 5 10 15

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194

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 <212> PRT  
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 Met Thr

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 Ser Val

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 Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met  
                           20                          25

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 Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu  
                           20                          25                          30  
 Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys  
                           35                          40                          45  
 Cys Arg Met Pro Arg Thr Leu Arg Arg Leu  
                           50                          55

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 Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

	5	10	15
Glu Cys			
<210> 549			
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<212> PRT			
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Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg			
	5	10	15
Gln Ala			

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<210> 550
<211> 14
<212> PRT
<213> Homo sapiens

<400> 550
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          5                               10

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<220>  
<223> Made in a lab

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5 10

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tcataccagt	ccacggacta	ttatgaacca	caccacacag	gaggagggtga	gcactaggca	180	
gcacaaggaa	gcttcacctg	tacttaacgc	cacacgccat	ggctcatatt	acagcgtgaa	240	
ctctgcctcc	atcagatca	gtgataacat	tagaaactca	ttggagcagc	aacctgtgtg	300	
tgaactgcct	atccgaagga	tctaggttgt	gtgcttcgta	tgagaatcta	atgccagatg	360	
atctatcatt	gtctcacttt	gcccccagat	aagaccatct	agttgcagaa	aaataagctc	420	
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&lt;210&gt; 553

&lt;211&gt; 58

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 553

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Ser Ile Cys Asn Met Thr Cys Ala Ser Val Phe Phe Cys Asp Gln Lys
          5              10              15
Phe Leu Thr Phe Ser Phe Leu Ser Met Val Glu Pro Pro Arg Ala Gly
          20              25              30
Val Leu Asn Ser Gln Ala Thr Asp Ser Tyr Gln Ser Thr Asp Tyr Tyr
          35              40              45
Glu Pro His His Thr Gly Gly Gly Glu His
          50              55

```

&lt;210&gt; 554

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 554

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Leu Gln Lys Asn Lys Leu Arg Ala Ser Thr Asp Ser Thr Leu Trp Ile
          5              10              15
Cys Ala Ala Glu Ala Ser Thr Lys Pro Tyr Phe Tyr Thr Cys Leu Val
          20              25              30
Met Leu His Gly Gln Gly Leu Ala Leu Leu Ser Pro Thr Asn Leu Pro
          35              40              45
Glu Ile Leu Arg Phe Leu Phe Asn Gly Phe Leu
          50              55

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197

<210> 555  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

<400> 555  
 Leu Gly Arg Phe Ser Leu Ser Cys Lys Ser Gly His Ser Arg Gly Gln  
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 Pro Gln Leu Gly Ala Thr Ala Gln Gly Lys Val His Met Gly Leu Ser  
                   20                  25                  30  
 Thr Ala Gln Gly Ser Ile Gln Asp Ile Lys Val Pro His Ser Ile Asp  
                   35                  40                  45  
 Leu Val Ala Lys Lys Lys Lys Gln Thr Leu Ile Ser Phe Cys His Pro  
                   50                  55                  60  
 Ser Asp Pro Leu Glu Leu Leu  
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<210> 556  
 <211> 81  
 <212> PRT  
 <213> Homo sapiens

<400> 556  
 Asn His Pro Glu Gln Gly Ser Ser Thr Pro Arg Pro Gln Thr His Thr  
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 Ser Pro Arg Thr Ile Met Asn His Thr Thr Gln Glu Glu Val Ser Thr  
                   20                  25                  30  
 Arg Gln Ala Lys Glu Ala Ser Pro Val Leu Thr Ala Thr Arg His Gly  
                   35                  40                  45  
 Ser Tyr Tyr Ser Leu Asn Ser Ala Ser Thr Gln Ile Ser Asp Asn Ile  
                   50                  55                  60  
 Arg Asn Ser Leu Glu His Glu Pro Cys Cys Glu Leu Pro Ile Arg Arg  
                   65                  70                  75                  80  
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<210> 557  
 <211> 54  
 <212> PRT  
 <213> Homo sapiens

<400> 557  
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 Glu Gln Ala Tyr Leu Ile Ser Ala Arg Glu Lys Thr Asn Asn Gly Leu  
                   20                  25                  30  
 Lys Gly Ser Leu Thr Met Lys Val Ser Ala Asn Ser Trp Leu Arg Cys  
                   35                  40                  45  
 Gly Phe His Ile Arg Phe  
                   50

<210> 558  
 <211> 77  
 <212> PRT  
 <213> Homo sapiens

198

<220>  
 <221> VARIANT  
 <222> (1)...(77)  
 <223> Xaa = Any amino acid

<400> 558  
 Asn Asp Arg Asp Arg Asn Ser Asn Lys Val Ile Xaa Lys Ala Asn Leu  
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                           20                          25                          30  
 Phe Thr Cys Thr Lys Arg His Lys His Leu Gln Cys Ser Ser Val His  
                           35                          40                          45  
 Leu Cys Lys Ile Pro Pro Arg Leu Lys Gly Arg Asp Lys Lys Lys Lys  
                           50                          55                          60  
 Pro Ser Tyr Leu Ser Gly Val Leu His Ser Arg Ser Tyr  
                           65                          70                          75

<210> 559  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

<400> 559  
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 Thr Asn Pro Val Val Asn Cys Leu Ser Glu Gly Ser Arg Leu Cys Ala  
                           20                          25                          30  
 Ser Tyr Glu Asn Leu Met Pro Asp Asp Leu Ser Leu Ser His Phe Ala  
                           35                          40                          45  
 Pro Arg  
                           50

<210> 560  
 <211> 56  
 <212> PRT  
 <213> Homo sapiens

<400> 560  
 Ile Gly Ser Leu Lys Gly Pro Thr Thr Ala Gly Ser His Cys Ser Gly  
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 Glu Gly Ser Tyr Gly Thr Phe Tyr Cys Pro Arg Phe Tyr Thr Gly Tyr  
                           20                          25                          30  
 Lys Gly Ala Ser Gln Tyr Arg Ser Gly Ser Lys Glu Glu Glu Thr Asn  
                           35                          40                          45  
 Thr Asp Leu Phe Leu Pro Pro Leu  
                           50                          55

<210> 561  
 <211> 57  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT

199

&lt;222&gt; (1)...(57)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 561

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Val Leu His Leu Asp Gln Met Asn Asn Val Gly Ile Xaa Met Asp Lys
              5              10              15
Gly Leu Lys Ser Pro Glu Ile Lys Asn Pro Ala Pro Thr Gly Thr Ser
              20              25              30
Asn Leu Ser Cys Phe Leu Ser Xaa Phe Trp Leu Met Gln Gly Thr Asn
              35              40              45
Ser Leu Pro Arg Glu Asn Tyr Leu Asn
              50              55

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&lt;210&gt; 562

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(59)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 562

```

Asp Leu Tyr Pro Xaa Arg Ser Gln His Cys Ser Phe Asp Pro Ser Val
              5              10              15
Ala Pro Met His Gly Ile Lys Asn Ser Ile Thr Ser Leu Ile Phe Leu
              20              25              30
Ile Ser Tyr Leu Xaa Leu Glu Met Ser Ser Leu Ser Glu Ser Leu Val
              35              40              45
Leu Ser Ser Gly Asp Tyr Val Leu Asp Thr Pro
              50              55

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&lt;210&gt; 563

&lt;211&gt; 79

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 563

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Cys Phe Leu Phe Pro Tyr Leu Trp Leu Tyr Ala Gln Pro Leu Phe Pro
              5              10              15
Lys Gln Gln Pro Pro Ala Leu Ala Pro Gly His Pro Asp Phe Ile His
              20              25              30
Thr Gln Asn Glu Gln Ile Asp Pro Ser Pro His Ile Gln Asn Leu Met
              35              40              45
Trp Asn Pro His Leu Ser Gln Glu Leu Ala Glu Thr Phe Met Val Arg
              50              55              60
Asp Pro Leu Arg Pro Leu Leu Val Phe Ser Leu Ala Asp Ile Arg
              65              70              75

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&lt;210&gt; 564

&lt;211&gt; 64

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 564

200

Ala Cys Ser Lys Gly Ser Glu Glu Phe Gln Arg Val Arg Gly Val Ala  
                                   5                                  10                                  15  
 Glu Arg Asp Gln Cys Leu Phe Leu Leu Cys Tyr Gln Ile Tyr Thr  
                                   20                                  25                                  30  
 Val Arg His Leu Tyr Ile Leu Tyr Arg Thr Leu Gly Ser Arg Lys Ser  
                                   35                                  40                                  45  
 His Met Asn Leu Pro Leu Ser Ser Gly Ser Gln Leu Trp Leu Ala Pro  
                                   50                                  55                                  60

&lt;210&gt; 565

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(57)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 565

Leu Tyr Tyr Cys Ser Tyr Leu Cys His Phe Arg Thr Ala Leu Ile Leu  
                                   5                                  10                                  15  
 Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln  
                                   20                                  25                                  30  
 Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu  
                                   35                                  40                                  45  
 Tyr Ala Val Ser Ser Xaa His Asn Val  
                                   50                                  55

&lt;210&gt; 566

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 566

Ile Leu Leu Glu Phe Phe Arg Asn Gln Arg Gly Ser Leu Asn Pro Arg  
                                   5                                  10                                  15  
 Lys Thr Val Pro Phe Ile Lys Ser Glu Gly Gly Glu Lys Lys Gly His  
                                   20                                  25                                  30  
 Cys Asn His Ser Val Val Ser Ile Asp Ser Ala Ala Ala Leu Leu Pro  
                                   35                                  40                                  45  
 Leu Lys Leu Val Leu Leu Pro  
                                   50                                  55

&lt;210&gt; 567

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 567

Tyr Ser Asp Phe Asp Val Phe Cys Ser His Thr Tyr Gly Tyr Met Leu  
                                   5                                  10                                  15  
 Ser His Cys Ser Gln Ser Ser Ser Pro Leu Leu Trp Pro Leu Gly Ile  
                                   20                                  25                                  30  
 Leu Thr Leu Ser Thr His Lys Met Ser Lys Leu Thr Leu Pro Pro Ile

201

35  
Phe Arg Thr  
50

40

45

<210> 568  
<211> 75  
<212> PRT  
<213> Homo sapiens

<400> 568  
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Tyr Val Ala Phe Asn Ser Val Pro Ser Thr Cys Leu Leu Ala Ser Leu  
20 25 30  
Thr Glu Thr Pro Val Thr Thr Ile Leu Thr Ile Ile Ile Asn Leu Thr  
35 40 45  
Cys Phe Gln His Ala Glu Ser Tyr Leu Phe Tyr Pro Leu Ala Asp  
50 55 60  
Phe Leu Leu Gln His Ile Ser Leu Gly Lys Leu  
65 70 75

<210> 569  
<211> 4809  
<212> DNA  
<213> Homo sapiens

<400> 569  
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&lt;210&gt; 570

&lt;211&gt; 951

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 570

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```

&lt;210&gt; 571

&lt;211&gt; 819

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 571

```

cagcttaaaa atggtttctt gaaatcagtg attagcattc actcaccagt acccctacta 60
aggggtaggc actggtttgt actcctggga atacaggagt acaccagaat ttattttctgc 120
ttattgcttt tgttgcaaat gccgtggctt catctgagga attctagaat tcagaggggtg 180
tagccctcca ctctgtctgc ttgctatctg ctctcattgc atccgtttta cctgcattct 240
gaaagatggt tctcaggttt ttccctgacg attttcttct tttctgattc tgacaatggt 300
ttaaatcatt gtactgtggt tatcatttct ctgcatttat tttaccatc ttcccttgta 360
acttgtccta ttgtctttta atttctgcct gttctttatg gctttcaact tcataaataa 420
catgttttct caaatctctt tgtgaattcc agagagggcc aggcacggtg gctcacatct 480
gtaatcccag cactttgggg aggctgagac ggggtggatca cttgaggtca ggagtttgag 540
accagcctgg ccaacatggt gaaatcccgt ttactataaa atacaaaaat taccaggcca 600
tggtggcggg cgcctgtaat cccagggtact cgggagggctg agggaggaga atcgcttgaa 660
cctgggaggg tgagggagga gaatcgcttg aaccggggag gcagaggttg cagtgaaccg 720
agatcatggt gctgcactcc agcctgggtc acagagcaag actctgcctc aaaaacaaac 780
aaataaacia acaacaaac aaaacagaga gattttgct 819

```

&lt;210&gt; 572

&lt;211&gt; 203

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 572

```

tatagaatac tcaagctatg catcaagctt ggtaccgagc tcggatccac tatttacggc 60
cgccagtgtg ctggaattcg cccttagctc ggatccacta gtccagtgtg gtggaattcc 120
attgtgttgg gcccaacaca atggagccac cacatccagc ctgccacata cttttaact 180
atcaggtctc atgagaactc atg 203

```

&lt;210&gt; 573

&lt;211&gt; 132

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 573

```

Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
      5                      10                      15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg

```

204

```

      20      25      30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
      35      40      45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
      50      55      60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
      65      70      75      80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
      85      90      95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
      100      105      110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
      115      120      125
Leu Leu Asn Tyr
      130

```

<210> 574  
 <211> 62  
 <212> PRT  
 <213> Homo sapiens

```

<400> 574
Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
      5      10      15
His Gly Gly Arg Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
      20      25      30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
      35      40      45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
      50      55      60

```

<210> 575  
 <211> 76  
 <212> PRT  
 <213> Homo sapiens

```

<400> 575
Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
      5      10      15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
      20      25      30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
      35      40      45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
      50      55      60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
      65      70      75

```

<210> 576  
 <211> 68  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT

205

&lt;222&gt; (1)...(68)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 576

```

Met Leu Gly Lys Ser Arg Ala Val Cys Leu Pro Ser Thr Thr Val Thr
              5              10              15
Thr Val Cys Tyr Leu Ala Ser Ser Ser Ala Ser Arg Glu Thr Ala Thr
              20              25              30
Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
              35              40              45
Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
              50              55              60
Pro Gly Tyr Ser
65

```

&lt;210&gt; 577

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 577

```

Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
              5              10              15
Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro
              20              25              30
Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe
              35              40              45
Arg Leu Ala Pro Pro Ala Asp Thr Pro
              50              55

```

&lt;210&gt; 578

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 578

```

Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His
              5              10              15
His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr
              20              25              30
Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His Ile Ala Lys Val Tyr
              35              40              45
Gln Pro His
              50

```

&lt;210&gt; 579

&lt;211&gt; 56

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 579

```

Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu
              5              10              15
Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr
              20              25              30
Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His
              35              40              45
Ile Ala Lys Val Tyr Gln Pro His

```

206

50

55

&lt;210&gt; 580

&lt;211&gt; 67

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 580

```

Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser
      5                      10                      15
Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro Leu Thr Phe Trp Lys
      20                      25                      30
Gly Lys Trp Val Gln Cys Cys Leu Pro Leu Trp Gly Leu Leu Gly Ser
      35                      40                      45
His Ala Phe Tyr Ile Tyr Ala Val Asp Ile Phe Met Phe Pro Gly Ser
      50                      55                      60
Phe Ile His
      65

```

&lt;210&gt; 581

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 581

```

Met Leu Glu Val Lys Phe Glu Val Ser Leu Arg Pro Thr Gly Asn Glu
      5                      10                      15
Thr Ala Gly Gln Thr His Gly Thr Gln Asp Lys Gly Ser Lys Asp Ser
      20                      25                      30
Thr Ala Ala Asp Ile Leu Cys Asp Ser Leu Glu Ser Ser Arg Pro Ala
      35                      40                      45
Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu
      50                      55                      60
Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser
      65                      70                      75

```

&lt;210&gt; 582

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 582

```

Met Leu Phe Leu Gln Thr Ile Asp Thr Lys Cys Thr Gly Ile Glu Ile
      5                      10                      15
Asn Arg Asn Trp Ser Lys Val Trp His Thr His Ser His Val Asp Val
      20                      25                      30
Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
      35                      40                      45
Leu Gly Val
      50

```

&lt;210&gt; 583

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 583

```

Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg

```

207

```

          5          10          15
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          20          25          30
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          35          40          45
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          50          55          60

```

&lt;210&gt; 584

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 584

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

&lt;210&gt; 585

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 585

```

Met Val Tyr Arg Phe Gly Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu
          5          10          15
Ala Ser Leu Gly Ser Ser Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp
          20          25          30
Arg Gln Ala Asp Pro Ser Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu
          35          40          45
Leu Phe
          50

```

&lt;210&gt; 586

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 586

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

&lt;210&gt; 587

&lt;211&gt; 1408

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 587

```

ctggacactt tgcgagggct tttgctggct gctgctgctg cccgtcatgc tactcatcgt 60
agcccgcccg gtgaagctcg ctgctttccc tacctcctta agtgactgcc aaacgcccac 120
cggctggaat tgctctgggt atgatgacag agaaaatgat ctcttcctct gtgacaccaa 180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240
gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa 300
tgagtgttac ctgacgacagg ctgcatgcaa acagcagagt gagatacttg tgggtgcaga 360
aggatcatgt gccacagatg caggatcagg atctggagat ggagtccatg aaggctctgg 420
agaaactagt caaaaggaga catccacctg tgatatttgc cagtttggtg cagaatgtga 480
cgaagatgcc gaggatgtct ggtgtgtgtg taatattgac tgttctcaaa ccaacttcaa 540
tcccctctgc gcttctgatg ggaaatctta tgataatgca tgccaaatca aagaagcatc 600
gtgtcagaaa caggagaaaa ttgaagtcat gtctttgggt cgatgtcaag ataacacaac 660
tacaactact aagtctgaag atgggcatta tgcaagaaca gattatgcag agaatgtaa 720
caaattagaa gaaagtgccg gagaacacca cataccttgc ccggaacatt acaatggctt 780
ctgcatgcat gggaagtgtg agcattctat caatatgcag gagccatctt gcagggtgtg 840
tgctggttat actggacaac actgtgaaaa aaaggactac agtgttctat acgttgttcc 900
cggctcctga cgatttcagt atgtcttaat cgcagctgtg attggaacaa ttcagattgc 960
tgtcatctgt gtggtggtcc tctgcatcac aaggaaatgc cccagaagca acagaattca 1020
cagacagaag caaaatacag ggcactacag ttcagacaat acaacaagag cgtccacgag 1080
gttaatctaa agggagcatg tttcacagtg gctggactac cgagagcttg gactacacaa 1140
tacagtatta tagacaaaag aataagacaa gagatctaca catgtgcct tgcatattgtg 1200
gtaatctaca ccaatgaaaa catgtactac agctatattt gattatgtat ggatatattt 1260
gaaatagtat acattgtctt gatgtttttt ctgtaatgta aataaactat ttatatcaca 1320
caatawagtt ttttctttcc catgtatttg ttatatataa taaatactca gtgatgagaa 1380
aaaaaaaaa aaaaaaaaaa rwmgaccc 1408

```

&lt;210&gt; 588

&lt;211&gt; 81

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 588

```

Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
                    5              10              15
Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys
                20              25              30
Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
                35              40              45
Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
                50              55              60
Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
                65              70              75              80
Ile

```

&lt;210&gt; 589

&lt;211&gt; 157

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 589

```

Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
                    5              10              15
Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu
                20              25              30
Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu

```

209

```

      35      40      45
Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
  50      55      60
Pro Val Ile Phe Ala Ser Leu Val Gln Asn Val Thr Lys Met Pro Arg
  65      70      75      *      80
Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile
      85      90      95
Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
      100      105      110
Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
      115      120      125
Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
      130      135      140
Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
145      150      155

```

&lt;210&gt; 590

&lt;211&gt; 347

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 590

```

Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
      5      10      15
Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser Gly Tyr
      20      25      30
Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr Cys Lys
      35      40      45
Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys Val Cys
      50      55      60
Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser Asn Gly
      65      70      75      80
Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys Lys Gln
      85      90      95
Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr Asp Ala
      100      105      110
Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu Thr Ser
      115      120      125
Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala Glu Cys
      130      135      140
Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp Cys Ser
145      150      155      160
Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser Tyr Asp
      165      170      175
Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu Lys Ile
      180      185      190
Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr Thr Thr
      195      200      205
Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu Asn Ala
      210      215      220
Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys Pro Glu
225      230      235      240
His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser Ile Asn
      245      250      255
Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly Gln His
      260      265      270
Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly Pro Val

```



		275					280				285				
Arg	Phe	Gln	Tyr	Val	Leu	Ile	Ala	Ala	Val	Ile	Gly	Thr	Ile	Gln	Ile
	290					295					300				
Ala	Val	Ile	Cys	Val	Val	Val	Leu	Cys	Ile	Thr	Arg	Lys	Cys	Pro	Arg
305					310						315				320
Ser	Asn	Arg	Ile	His	Arg	Gln	Lys	Gln	Asn	Thr	Gly	His	Tyr	Ser	Ser
				325						330				335	
Asp	Asn	Thr	Thr	Arg	Ala	Ser	Thr	Arg	Leu	Ile					
			340					345							

```
<210> 591
<211> 565
<212> DNA
<213> Homo sapien
```

<400> 591						
actaaagcaa	atgaacaagc	tgacttgcta	gtatcatctg	cattcattga	agcacaagaa	60
cttcatgcct	tgactcatgt	aaatgcaata	ggattaaaaa	ataaatttga	tatcacatgg	120
aaacagacaa	aaaattattg	acaacattgc	accaggtgtc	agattctaca	cctggccact	180
caggaagcaa	gagttaatcc	cacaggtgta	tgctctaatt	tgttatggca	aatggatgtc	240
atgcacgtac	cttcatattg	aaaattgtca	tttgtccatg	tgacagttga	tacttatcca	300
catttcata	gggcaacctg	ccagacagga	gaaagtactt	cccattgtta	aagacattta	360
ttatcttggt	ttcctgtcat	gggagttcca	gaaaaagtta	aaacagacaa	tgggccaggt	420
tactgtagta	aagcatttca	aaaattctta	aatcagtgga	aaattacaca	tacaatagga	480
attctctata	attcccaagg	acagggcata	attgaaggaa	ctaatagaac	actcaaagct	540
caattggtta	aacaaaaaaa	aaaaa				565

```
<210> 592
<211> 188
<212> PRT
<213> Homo sapien
```

<400> 592															
Thr	Lys	Ala	Asn	Glu	Gln	Ala	Asp	Leu	Leu	Val	Ser	Ser	Ala	Phe	Ile
1				5					10					15	
Glu	Ala	Gln	Glu	Leu	His	Ala	Leu	Thr	His	Val	Asn	Ala	Ile	Gly	Leu
			20					25					30		
Lys	Asn	Lys	Phe	Asp	Ile	Thr	Trp	Lys	Gln	Thr	Lys	Asn	Ile	Val	Gln
		35					40					45			
His	Cys	Thr	Gln	Cys	Gln	Ile	Leu	His	Leu	Ala	Thr	Gln	Glu	Ala	Arg
	50					55					60				
Val	Asn	Pro	Arg	Gly	Leu	Cys	Pro	Asn	Val	Leu	Trp	Gln	Met	Asp	Val
65					70					75					80
Met	His	Val	Pro	Ser	Phe	Gly	Lys	Leu	Ser	Phe	Val	His	Val	Thr	Val
				85					90					95	
Asp	Thr	Tyr	Ser	His	Phe	Ile	Trp	Ala	Thr	Cys	Gln	Thr	Gly	Glu	Ser
			100					105						110	
Thr	Ser	His	Val	Lys	Arg	His	Leu	Leu	Ser	Cys	Phe	Pro	Val	Met	Gly
		115					120					125			
Val	Pro	Glu	Lys	Val	Lys	Thr	Asp	Asn	Gly	Pro	Gly	Tyr	Cys	Ser	Lys
	130					135					140				
Ala	Phe	Gln	Lys	Phe	Leu	Asn	Gln	Trp	Lys	Ile	Thr	His	Thr	Ile	Gly
145					150					155					160
Ile	Leu	Tyr	Asn	Ser	Gln	Gly	Gln	Ala	Ile	Ile	Glu	Gly	Thr	Asn	Arg
			165						170					175	
Thr	Leu	Lys	Ala	Gln	Leu	Val	Lys	Gln	Lys	Lys	Lys				
			180					185							

211

<210> 593  
 <211> 271  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(271)  
 <223> n = A,T,C or G

<400> 593  
 actttatgtt cnagtgcana aancncctg gattgccacc ntactctcag ggctgtgant 60  
 tgtgcnccca nagcaacctg ggcacgcggg gacagggggg ccnacaattg agggagcggg 120  
 gtccctagct ggggtctata catgncnggg naagggcngc tgagtnccat nagcaaagga 180  
 nctagnatnt gcgggggtgc ggcctgggcc taccctttna agcatccntn gatccactcc 240  
 angaancng gggtagncag gtttnccaac a 271

<210> 594  
 <211> 376  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(376)  
 <223> n = A,T,C or G

<400> 594  
 cctttggggg nggggggaac ctttaccatt gtncccttt atttcatttg gttnggggtc 60  
 gcgcctcnn gggccaacaa agttatcgtn nttgaagaga anattttttt ggnttngncc 120  
 cgattaagcg ncaaatgtgt agcaaaangc cgtgccactt gtggcgtagc tncgtcgggt 180  
 cgattcgacg acaaggcgtn gcgcgntanc gttagtctcn aatngaccn gtggcatgag 240  
 cccacgangg ntctgtgtcg tcacatggnc tctagacata acgncncn ttttttncag 300  
 agggggntgc cgcccttagg gaggnagggg tggggacact agccaancca nantctnacc 360  
 ccattgaaga aaaggn 376

<210> 595  
 <211> 242  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(242)  
 <223> n = A,T,C or G

<400> 595  
 agnctgctgn tcgtnccctn tatgtggctt catnntgagg acaanagtng cactgaggct 60  
 tgnngnatgc aggcaaggnc aagctggctc aaaaagcatc caccacctc tgnaangggg 120  
 atgccangag cangtgcacc agtcccaact angagnccn ggcatgntac atcttcttcc 180  
 acccctnaaa ntttngtcta caangnccat ttttctttt ctcttaaggg ncnctggct 240  
 tc 242

<210> 596  
 <211> 535  
 <212> DNA  
 <213> Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(535)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 596

accagttgga	tactgctaaa	nagatattta	tgacgcctca	tatgttaagt	cgtatatttt	60
gaaagctttt	taaatttttt	ctttaagaag	atttttagatg	cttatcactg	agtaccagag	120
ggatgtaggc	tgatgccctt	atcaacaaag	tcaggggactg	tggcacacaa	ggattgacta	180
ctgcagacac	ggccacaatg	ctacctctag	agggcctgaa	tccccctgcc	ctctctgggtg	240
gggagaaggg	ctggcagagc	cattagcatg	ggctccggcc	aatcctggcc	actttgacac	300
tcctgggtgct	gacccagggt	cctggaggaa	gggatgaggt	gggcagtaga	gatgctcagg	360
gcagtggccc	ctttccatcc	acactggaac	tatttcagta	ttttaccacc	aattcagcca	420
ttcccttggtg	cgctggctga	acatcagccc	tgctccaggt	ctcagtttcc	cctttgtaaa	480
gggaaagctc	tggattcagg	gagtgatgaa	gaggtcatca	tggtcttgag	aattc	535

&lt;210&gt; 597

&lt;211&gt; 257

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(257)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 597

tttcnatacc	caaaantacc	ccatattang	accanacatt	tgctctnggaa	aaattaccat	60
tntntaacnt	ttgggccacc	tgagannaaa	tggtgtgaat	ncatgataag	atggancagn	120
atttctctta	agatnngatn	agaccccggt	tttcacggaa	catatccaag	nacccaatag	180
gnaacaagcc	acgggngggag	tcacaaacat	atattcttta	ctctcataat	ccgtnnccaca	240
naactnttgn	acttgac					257

&lt;210&gt; 598

&lt;211&gt; 222

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(222)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 598

nntggntacc	gtcnaaactt	nncttggtac	ccgagctcgg	atccactagt	ccagtgtggt	60
ggaattccat	tgtgttgggc	tataagctgt	aatagtggag	ncgtgctngg	ttcattgcan	120
nagnccctcc	gcanncacnc	ttgnnacaac	ctgtgagnag	gcataaatt	attcacataa	180
tcactactgc	atgaanctga	ctcaaacgca	tccacntaca	cc		222

&lt;210&gt; 599

&lt;211&gt; 238

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(238)

213

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 599

gcatgacatc	ancgatgtnt	ttggnnacct	ganattngct	aaaactngng	natgccgggn	60
atgnagggtt	ggtantgatc	tatgcactca	catctcatgg	ggacgtttca	tgtggagtgn	120
tcgacaangt	tgctgnancn	gagaagtgat	gatctcagtt	gaaaggggtca	tgtgaataca	180
cnttacactt	gaaaaagaag	cacattggga	atatcacgaa	acgnccacca	acatcctg	238

&lt;210&gt; 600

&lt;211&gt; 232

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(232)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 600

cgaactattt	agactaccta	ggaaaattat	tttagtatca	gaagaatata	aggggtgtag	60
tactcatcag	agctaaatga	gagcgcttta	aaaatgttag	tttgtcttcc	gccattttcta	120
cagaaagctg	caatttcagg	ttttcaacct	aataggtgat	atttaanaaa	aaaaaaaagc	180
aatcgcaaat	agccccactg	cttttaca	tcattttttc	cccaacacaa	tg	232

&lt;210&gt; 601

&lt;211&gt; 547

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(547)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 601

catttgtgtg	gggaaaaaat	gatttgtata	agcagtgggg	ctatttgcca	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aacctgaaat	tgacgttttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcathtag	ctctgatgag	tactacaccc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagttag	taactcaaaa	cgagtgcata	tnggaagtat	cgcagccggt	300
nctggatnaa	attcccagct	tgctngcttg	ctnagccggg	ggcggttnaa	aaaaacatct	360
gcagcccngg	ggnaaaaacc	ttcgattgtg	tcttacgtgt	ttacgttatt	ttatttccct	420
nnagcaaggc	nggganttgg	ggactcgaaa	tggtacagtt	gggctgggga	tcgcccttgt	480
tacataaaaag	ncgtccagaa	gagggacggt	tacaggcngg	ganctccaaa	ggtcagtcct	540
tgccatt						547

&lt;210&gt; 602

&lt;211&gt; 826

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(826)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 602

cggggggnnt	tacgtctctc	tggacgtttt	tattgtacca	ggcgatccc	agcccaactg	60
------------	------------	------------	------------	-----------	------------	----

214

```

taccattcga gtccctactc ctgccttgct ctagggaaat aaaataacgt aaacacgtaa 120
gaacaatgcg aaagcgtttt cttccctagg ctgcagattg tcttcttcac cgcccctgct 180
tagctagcta gctagctggg aatttaatcc agaaacggct tgcgatacct cctagatgca 240
ctcgttttga gttacaaact ccgcggtatta catgtctttt taaaaaagtt tagactacac 300
tagggaaaat tatttttagta tcagaagaat atcagggggg gtagtactca tcagagctna 360
atgagagcgc tttaaaaatg ttagtttgct ttccgccatt tctacagaaa gctgcaattt 420
caggttttca ncctaataagg tgatatntaa gaaaaaaaaa acaatcgcan atagcccact 480
gcttttacia atcatttttc tcttctagggt atagcctgtc aggtggccta atgtattttt 540
gacatctcta ggaattttta tagaccagaa atgggtgccg gagatatgcc tgcactaatc 600
ttaagtgggg atttatgtat ttctcaanca agtgattaaa gcaaaactag gcacgaatga 660
aatcaagatc tttaggccag aatcatgaa nanttttana attattttan gaatctgtgg 720
cttctcttct taaaatngaa aaaaaaattg tttaaaccca naaggtctga atacccaagc 780
nccctgaacn anagaacaan gccggagcac cccctcccaa atcccc 826

```

```

<210> 603
<211> 817
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(817)
<223> n = A,T,C or G

```

```

<400> 603
nnangacttt tgtggtntta tacaattntt ttttctatct ctatgaagag aaagccacag 60
agtcctaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa 120
tcgtgcctag ttttgcttta atcacttgct tgagaaatac ataaatcccc acttaagatt 180
agtgacggca tatctctggc acccatttct ggttctatta aaattcctag agatgtcaaa 240
aattacatta ggccacctga caggctatac ctagaagaga aaaaatgatt tgtaaaagca 300-
gtggggctat ttgcgattgc tttttttttt tcttaaatat cacctattag gttgaaaacc 360
tgaaattgca gctttctgta gaaatggcgg aagacaaact aacattttta aagcgctctc 420
atttagctct gatgagtact acaccctga tattcttctg atactaaaat aattttccta 480
gtgtagtcta aactttttta aaaagacatg taatccgcgg agtttgtaac tcaaaacgag 540
tgcattctagg aggtatcgca agccgtttct ggattaaatt ccagctagc ttgcttgctt 600
agcagggggc ggmaanaaag acatctgcag cctagggaag aaaaccttct gcattgttct 660
tacgtgttta cgttatttta ttctctanaa caaggcngaa ttgggactcg aatggttcag 720
ttgggggtgg ggatcccctg gtncataaaa ngtcanaaag anggtacagg cggaacncca 780
agggctcgcc tgcatttana ctcggaattt tgggtgcc 817

```

```

<210> 604
<211> 694
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(694)
<223> n = A,T,C or G

```

```

<400> 604
cttttcaaat catttttnct cttctaggta tancctgtca ggtggcctaa tgtaattttt 60
gacatctcta ngaattttta tagaaccaga aatgggtgcc agagatatgc ctgcactaat 120
cttaagtggg gatttatgta tttctcaagc aagtgattaa agcaaaacta ggcacgattg 180
aatcaagat cttttaggca anaaagtcag gatgagtttt agaattattt taggactctg 240
tggttttctc ttcatagaaa tagaaaaaaa aattgtataa aaccacaaaa ggtcctgaat 300
agccaaagca acactganca aaaagaacan agcaggggaag caacacacta ccngaattca 360
aattatacta ccagggtgta gtaacaaaaa cagcattcta ttggcataaa atagacacca 420

```

215

```

agaccaatgg ancagaataa agaacccccac aaataaatcc atatatntac cgccanctga      480
ttatcaataa cnaacaccaa gaacatatnt taagggaacnt nctattcaat aantagtgt      540
ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agaccctat ccctcaccat      600
acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact      660
atnaaancta ctattaagaa aacagatcnc nccc                                     694

```

&lt;210&gt; 605

&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(678)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 605

```

taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt      60
actcatcana gctaaatgag agcgctttaa aaatgttagt ttgtcttcgg ccatttctac      120
agaaagctgc aatttcagggt tttcaacctata taggtgata ttttaagaaa aaaaaaagca      180
atcgcaataa gcccactgc ttttacaat catTTTTTct cttctaggta tagcctgtca      240
ggtggcctaa tgtaattttt gacatctcta ggaattttaa tagaaccaga aatgggtgcc      300
agagatatgc ctgcactaat ctttaagtggg gatttatgta tttctcaagc aagtgattaa      360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt      420
anaattattt taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata      480
aaaaccacaa aaggtcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga      540
agcaacacac taccggaatt caattatact accaagggtg antaaccaaa acagcattct      600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaaataaat      660
cctatatatta cngcccncc                                     678

```

&lt;210&gt; 606

&lt;211&gt; 263

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(263)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 606

```

gtggggctcng canagccaa ctcagcttcc tttcgggctt tgttagcaga cggatcatcc      60
tctagtccac tgtgntcaaa ttccattgtg tgggggccnc tcgcctcggc canagatctg      120
agtgancana cntgtcccca ctgagggtgcc ccacagcngn ttgtnttcag cangggctna      180
caactcgacc ggcagcgan ggctggcaga antgngcgcc tnnctcattc ctacgcngtn      240
ngccgcagga aggangacag gcc                                     263

```

&lt;210&gt; 607

&lt;211&gt; 22

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Primer

&lt;400&gt; 607

```

ccatgtgggt cccggttgct tt                                     22

```

216

<210> 608  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 608  
gataggggtg ctcaggggtt gg

22

<210> 609  
<211> 40  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 609  
gctggacagg gggcaaaagc tggggcagtg aacctgtgc

40

<210> 610  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 610  
ccttgtccag atagcccagt agctgac

27

<210> 611  
<211> 46  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 611  
gatagagaaa accgtccagg ccagtattgt gggaggctgg gagtgc

46

<210> 612  
<211> 40  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 612  
gcacatgggt cactgcccc gcttttgccc cctgtccagc

40

<210> 613  
<211> 38  
<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 613

gccgctcgag ttagaattcg gggttggcca cgatggtg

38

<210> 614

<211> 53

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 614

cgcggggcat atgcatcacc atcaccatca catcataaac ggcgaggact gca

53

<210> 615

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 615

gcactcccag cctccacaa tactggcctg gacggtttcc tctatc

46

<210> 616

<211> 1350

<212> DNA

<213> Homo sapien

<400> 616

atgcatcacc atcaccatca catcataaac ggcgaggact gcagcccga ctcgcagccc	60
tggcaggcgg cactggtcat ggaaaacgaa ttgttctgct cgggcgtcct ggtgcatccg	120
cagtgggtgc tgtcagccgc aactgtttc cagaactcct acaccatcgg gctgggcctg	180
cacagtcttg aggcgacca agagccaggg agccagatgg tggaggccag cctctccgta	240
cggcacccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac	300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc	360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc	420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac	480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc	540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc	600
ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc	660
actgagtgga tagagaaaac cgtccaggcc agtattgtgg gaggctggga gtgcgagaag	720
cattcccac cctggcagggt gcttgtggcc tctcgtggca ggcagctctg cggcgggtgtt	780
ctgggtgcacc cccagtggtg cctcacagct gccactgca tcaggaacaa aagcgtgatc	840
ttgctgggtc ggcacagcct gtttcatcct gaagacacag gccagggtatt tcaggtcagc	900
cacagcttcc cacaccgct ctacgatatg agcctcctga agaatcgatt cctcaggcca	960
ggtgatgaat ccagccacga cctcatgctg ctccgcctgt cagagcctgc cgagctcacg	1020
gatgctgtga aggtcatgga cctgcccacc caggagccag cactggggac cacctgctac	1080
gcctcaggct ggggcagcat tgaaccagag gagtctctga ccccaaagaa acttcagtgt	1140
gtggacctcc atgttatttc caatgacgtg tgtgcgcaag ttaccctca gaaggtgacc	1200
aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa gctggggcag tgaaccatgt	1260
gccctgcccg aaaggccttc cctgtacacc aaggtggtgc attaccggaa gtggatcaag	1320



gacacccatcg tggccaaccc cgaattctaa

1350

&lt;210&gt; 617

&lt;211&gt; 449

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 617

```

Met His His His His His His Ile Ile Asn Gly Glu Asp Cys Ser Pro
 1           5           10           15
His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe
          20           25           30
Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His
          35           40           45
Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu
          50           55           60
Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu Ser Val
          65           70           75           80
Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu
          85           90           95
Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile
          100          105          110
Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu Val Ser
          115          120          125
Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys
          130          135          140
Val Asn Val Ser Val Val Ser Glu Glu Val Cys Ser Lys Leu Tyr Asp
          145          150          155          160
Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln
          165          170          175
Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly
          180          185          190
Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala Pro Cys Gly Gln Val
          195          200          205
Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys Phe Thr Glu Trp Ile
          210          215          220
Glu Lys Thr Val Gln Ala Ser Ile Val Gly Gly Trp Glu Cys Glu Lys
          225          230          235          240
His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala Val
          245          250          255
Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala His
          260          265          270
Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu Phe
          275          280          285
His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe Pro
          290          295          300
His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg Pro
          305          310          315          320
Gly Asp Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu Pro
          325          330          335
Ala Glu Leu Thr Asp Ala Val Lys Val Met Asp Leu Pro Thr Gln Glu
          340          345          350
Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile Glu
          355          360          365
Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu His
          370          375          380
Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val Thr
          385          390          395          400

```

219

Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Trp Gly  
                   405                  410                  415  
 Ser Glu Pro Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val  
                   420                  425                  430  
 Val His Tyr Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro Glu  
                   435                  440                  445  
 Phe

<210> 618  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(385)  
 <223> n = A,T,C or G

<400> 618  
 ctgtgctgag aaccaaagc tatgancact gcttttccaa atgtccataa naccaacatt 60  
 tttatcacta ccaccatcac ctgggagctc nttagaaagc tagtctcccg ggcaccaccc 120  
 tggcctactg aacctaattgt gcattttaaca agattnacgt ngaaatctgc aaagcacagg 180  
 ggongataac agtaccacct gntctggttc ctanccccan gacccttaca gtctaactgg 240  
 gacacaaggg cttnaaatca aattgcctat cattaagata tacaanganc ntgagaaact 300  
 gctncactta tntattaagg ngctctaaga cttagaaacn aaangcantg ctgagangat 360  
 tcaaatatga ngggggnac tttnc 385

<210> 619  
 <211> 869  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(869)  
 <223> n = A,T,C or G

<400> 619  
 gatatcccgga gaattcgagg ccgcgtcgac ctctacttgt ttagacataa atgcagtcta 60  
 gcattaaaga tcctttaaaa aaatgttttc ccaatgggta aaagacaagc tcaaataaat 120  
 gaactctcat acatatgcc aattgatga gtagataaat atttcagtag gtagttacta 180  
 gctttctgtg tatgagtaaa catatgggag aaattttaaaa cactaaagta gactcaatga 240  
 aagcatagta tcctatgtat tcgtttttca gaaatgtcta atgaaggaag gaaacaatga 300  
 atgaatgccc ttattcctct tagagtgtcg ggacatgggt ttgcctgaaa acttcatgtg 360  
 aattttatat tttgtacac attacacca tcttagactt atacgtataa gacataaggc 420  
 atatcttatg tcttcatgt ataataatct aagcagaaca aaaaataacg aaatattttc 480  
 ttccccaat ttttgagaca gatggatttt ccggaaagat gtgttttagct tttaatcctg 540  
 tggttttgtg taccacctgg cacactagag tgttgctcta attcagtgag ttgtaactct 600  
 ggggtaacag tggaaatact agggtagact ttaaaaatgc taatgctcgg gcctcgctga 660  
 agaccaaatt aattggaatc tctgngggng gnattgatct ttttataatc tttctanang 720  
 attctaattg gcttcaggg atgaaaacn ctgntggagc tnggaacctt cctttagttt 780  
 ggagaaaccc cgatgagggt ntnttaggcn ccgcctnttt ttggcctggg cttccccct 840  
 tatntntttt tggaangnnc cnaattttt 869

<210> 620  
 <211> 339  
 <212> DNA

220

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(339)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 620

gngcgggcct cncctgtgctt gctctcgctg ccgacgtctt tttccacca gctgtaggan	60
aagcccgaag accactggctc ccccgggtag cccaagtacc actggctcctc ctggctcctg	120
acgctncggg tcttcctcgt ggcgtagact gccagcttcg gagaccctc agccctccc	180
cgcttttctc caccacagga ggccatcagt agcgagctac tgctcggcc acaacctccc	240
agcangatag cccgcgggtt ccaatctgcg aaaggaggac cgccnagccc gaaatgccna	300
gccagcnat cactgccacg ccgagccnag cgctcgtgc	339

&lt;210&gt; 621

&lt;211&gt; 267

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(267)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 621

gggngcatg gtcccnggta gccaaagtaca tggctcctcct ggctcctgac gctacgggtc	60
ttcctcgtgg cgtagactgc cagcttcgga gacctcctcag cccctccccg cttttctcca	120
ccccaggagg ccatcagtag cgagctactg cctcggccac aacctcccag caggatngcc	180
cgcggtttcc aatctgcgaa aggaggaccg ccnagccaga aatgccnagc cnagcgatca	240
ctgccacgcc naggcnagcg ctctgtgc	267

&lt;210&gt; 622

&lt;211&gt; 847

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(847)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 622

cttangntgt cgactgacgt catgcatgan ttaaagcaga ggtttggtga aatttatgaa	60
aaatacaaaa ttccggcttg tcttgaggaa gagccactac ttgataactc tacaagagga	120
acagatgtga aggatattcc ctttaatttg acaataaaca tacctggttg tgaggaagaa	180
gatgcatctg aaatatctgt ctcatgggta ttcgagacat ttctgaaca aaaagaacc	240
agtctcaaaa atatcatcca tccatactat catccgtact ctgggtccca ggaacatgtt	300
tgccagtcac cttctaagct tcatttacat gaaaataaat tagactgcga caatgataac	360
aaactaggca ttggacatat ttttagtaca gataacaact ttcataatga tgcaagcact	420
aagaaagcaa ggaaccacga agtggttacg gttgaaatga aagaagacca agagtgtgat	480
ttgcaaatga caaaaaatat gaaccaaaat agtgacagtg gcagtacaaa taactataaa	540
agcctgaaac cttaaattaga aaatctgagt tctttaccac cagattctga cagaacatca	600
ggaagtatat ctacatgaag aattacagca agacatgcc aagtttaag aatgangtca	660
acacattaga aanaagantt ctgggctttg aagaaagaaa atgtccact tcataaagaa	720
ggttgaaaga agaattggag agccnngaan tttttgccn gaaattttcg ggaaccctac	780
tggtatgggtc nactggttgg ccatgaatga ataattgact aatcnnccaa ttcctnngga	840
agggaat	847

221

<210> 623  
 <211> 681  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(681)  
 <223> n = A,T,C or G

<400> 623  
 aaaactgtac tcgcgcgctg catgtcgaca ctagtggatc caaagaatcg gcacgagcga 60  
 aaangctcan gcagcccggc tggccgcccgc cgctcctccc cccaggaaaag ccaangtgga 120  
 ngctgatgtg gctgcangag ctcgtttcac agccctcan gtgganctgg ttgggccgcg 180  
 gctgccangg gcggaagtgg gtgtcccan gtctcagccc caaggctgcc cctcacaag 240  
 cactggtggt ttgcctccac tgccaccttg ggctccgaac ccgctcccct gctgtggang 300  
 cccaccgtgg gaatccaggt ccccaggtgg actgcctgcc ttgccctcac tgcccactct 360  
 gccacactt ccctgcctag anaccgggaa ggggctgtgt cggtantggt gccacctgg 420  
 atgtggcagc accgactgtg ggggtggacc tggccttgcc ggggtgcaaaa gtggggggccc 480  
 ngggaaaagc acctgaagtg gccctgaaaa atccccctt aattttncct caatttgggg 540  
 ctcaacaaa aggaaattgc tgaagccaan ggtaccaagg tcacccttaa ggccagggtg 600  
 aaaaggtccc aaaattccaa tccccacct ttgggcttnc ctcttggaac cccggcccc 660  
 tctcntgaan ttttaaaaaa n 681

<210> 624  
 <211> 661  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(661)  
 <223> n = A,T,C or G

<400> 624  
 attggtctta ctgtaccacc ggggtggaat cgatggccgc ggcgtctaaa tatccgattt 60  
 tttttttttt tcctcttctg actgtccatg gacaaatgaa actaacttaa tctaactaaa 120  
 aaacacaact atattttgaa gattttctat ctgcactcaa ggacactttc caccnccgttg 180  
 ttgttacctt ttggtcttgt ctctgaacat gaaattnatc tcaagggtatt ngatttctgg 240  
 acctcctatt cctgctatgg gtttgatatt tcttgggctc caggggccact gttgcattgg 300  
 gntgacagnt acctcctagc ccatanccct ctatcttggg aaacaaacct aacaactacg 360  
 tgtaccttcc atagatctct gattgagtct cagtatnccg ttgctcatgg gcgattcact 420  
 tgaatccgtn attggtgcca acaatcctga ctcatggggn aatggatcct atcacgttcc 480  
 cctgattngc aaccctgtg tacatanatc taatcgcata gaatctagcn tnggntatgc 540  
 gcggctacgc tatcaggnt tgntaactat ngcatggcta cgaancctga tcatgatcna 600  
 gggcatgga ctcttatcag ggggggttggg ccgngcttct ttttcnnacc ttggtaaaac 660  
 c 661

<210> 625  
 <211> 181  
 <212> DNA  
 <213> Homo sapien

<400> 625  
 gcaacaatca gatcatgtta aagtaaatct ccattgccct ggatcacttc aggatttaat 60  
 tgtccaagga gagcagggtt ctcctgtgaa aaaaaggtgg ggaaatgttt gagagtataa 120  
 aatacaaaat tcaaccgggtc gaaaatacac cactccattc agtgctctac ccccataagc 180

222

c 181

<210> 626  
 <211> 181  
 <212> DNA  
 <213> Homo sapien

<400> 626  
 gcaacaatca gatcatgtta aagtaaactc ccattgccct ggatcacttc aggatttaat 60  
 tgtccaagga gagcagggtt ctctgtgaa aaaaagggtg ggaaatgttt gagagtaaaa 120  
 aatacaaaat tcaaccggtc gaaaatacac cactccattc agtgctctac ccccataagc 180  
 c 181

<210> 627  
 <211> 813  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (813)  
 <223> n = A,T,C or G

<400> 627  
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 gtgagcagag gagaacttgc gatggcaaag ttaaaaacaa gaggagatga tggctctggg 120  
 gtggcacagg atgttaaaaa aattctcctg tccttaagga gttactgcta tttgagtaat 180  
 gtgccacttc cctacatagc cttctatgca gaaatgctat atttccactt cacaacccag 240  
 aacgtgcatt ttattttaca tttagaggag gaacaacaa ccagaaggca aaaactgggtg 300  
 cattattttt tgcaattctc ttggaaagag ttcgttttta acttctgctc agacagcaca 360  
 caactactgg gaatatatth taatttcaaa tctgatgtgt gacatctggg aactcattta 420  
 ttgctaataga agttttcaca ggaagcagca gtcaccagta gctcatctta tttttcagtt 480  
 ggcaaagtgt tgtttacctt ttattggcct gcatcgggtg ctcttatcac aggatattta 540  
 attagaaaac gcaagtagcc taacatagaa nagaatgga gtggtagata atagtagata 600  
 gaatggctaa atatttttat tacagtgatg taatatcact gnaatttatg gttaaaaatt 660  
 atgtaatact caaaaggaa tctcagactg gcgaaacagc tggnaacag cnttcacagg 720  
 gctttanact cctnttgagc tttccccctg ntggacttta gtcttccttt tacncccgna 780  
 gttncattn nttaccaatt gtnccgggaa ana 813

<210> 628  
 <211> 646  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (646)  
 <223> n = A,T,C or G

<400> 628  
 tttgggnggn ggtgtctcnt ttgggtggac tttttgggtc gtagggcccc aaggccgtta 60  
 atcccgtaat aacggaagac gaagaagagt cagaagagtg cttctataag gatcgggacg 120  
 agactacctt agaggaataa aggaaaaaag cagaggagga agagtgttag aaggagtcag 180  
 aagaacacca cacgtcgttc tgacactgga gccttatcaa aaaggcttag ataaacgata 240  
 gcgatctcga tatcgagctc aagaggtagg tttagagact tctcgtcctc gagagcgaaa 300  
 ttgaagatct cgacgacgat aagaagttaa agtgtagagg gtgcttgagg agcgcgtgga 360  
 aggattctgc ggagggaccc atcgacgtag agacttgaag gcctactaag gtccacaaga 420  
 agccccgctc tttctccgaa tggtcggagc gtacagtatg cgacgtcgat cggcagacaa 480

223

gctggcggtgta gactcgaagt gttcggggcga atcgacttat aatagtcgcg cgctagtaac	540
gtaggaacac gaagagtagt cgaaagaaaa cgtttagtga gggaaaagat tagggaaaaa	600
ggagaggctt aataactaag acacttggag cctaggccaa cgcgaa	646

&lt;210&gt; 629

&lt;211&gt; 617

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(617)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 629

gccccnccc ccctcctngg gcttatnngg acagaccac gtagtactct aaatcttctc	60
ctacgccgga caacggaccc tataccaatt cgaatcttgg aactccgac cgccggattc	120
tcttcccctt tcggcttccc ctttctgtcg gtaccctcc ctagtctct cctacacctt	180
cgtaccgtcg atatatagtc gccgcggact agcctattta ggtgtcctag actcgttatt	240
gatccactca ttagtctagt actatgcgtc acgtatctta gttgcctaag agggagatta	300
aatcctccac aagttccgac gaattcctgg actctcgtag tagcaaaactt tcttatgagg	360
cttccttgta tatcttctgg atgtttctcg tgtcccggtc ctccgctact actagagctc	420
cttgccctat ctctagaagt agaggactct cgggttcgtt ctccaaatct agcgttagag	480
ctatcgctac ccgctcgatt cccccagcgg aatcttgaaa cctgaggtag tacacaaacc	540
ctcncatct tcctcgggtt gctccttctt etcatcccc cttccgcct tctcggaan	600
gaatctactt tancttc	617

&lt;210&gt; 630

&lt;211&gt; 644

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(644)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 630

cnntcggcnt gggttttntt ctgagnnnc ccccccccc ccccccaaa cttacacca	60
caaacactt tcgccccct acctaggaga cattagaagg gtttaggctt cggcgtatag	120
taaagtctc tacctcgga gtagagaatt cggtatatta attcagggtt agaggctcgc	180
tcgttagatt tatagtttag gtttagaatc ggaaacctc gatcttcctt agaagggtaa	240
taagttaggc cctaaatccg tctaaccaag gcgttaaggt ccgtacctaa acctagtctt	300
atcttctatc aggcgcacca atataggtag gttctacttt cgtataggcc ttaaggaata	360
gttcggtagt tatcgaaggc actcctctct aggcctaggct tttctcagtc ttagtactcc	420
gggaccgtcg tcgcanaaat atcgatggac ggtaggatc tccgcgttac gcgtcgggct	480
agggatatag agcgaattat cggcgagagg cggtcgctan gaatcggtat caatatgntg	540
ttctttacc tacggatatc ggagaaaaac ataaaacctt ctnaccangg ataagggtt	600
atcggacccc taaaataaca gtaacattta gantactagt accc	644

&lt;210&gt; 631

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(526)

<223> n = A,T,C or G

<400> 631

cctcggcgtt	gggttttttt	ctgagccccc	ccccccccc	ccccccccc	ccccccggc	60
cccatagccc	caccggnccc	acccaaattt	taacaaaata	aatntaccta	tcgntcacct	120
atcccnegta	tcgngtaggt	cggtagccgt	accgngatc	ncnacgattn	ttcgggtcgt	180
cnccttaan	acggncccg	agcnccgga	anaaatacta	cgagngactc	taatntagca	240
anacccgccg	tcnattanta	gcacccctag	tcttccaatg	ncgnggattn	ngaatacctn	300
naagttatcg	ggtagaacgg	gtcccgggtc	cccgcctct	ttncaatata	cgccgggtac	360
aaantcgggt	tctaaattcc	ncacgaattt	ngncggcaac	attcncgggn	ccttattanc	420
cntttccaac	cccgatcnc	nagctcgatc	gggctttanc	gaatccgggg	tcnccccga	480
ngantccggg	tcctttgagt	ngctctagga	cggttacgac	ggagga		526

<210> 632

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(647)

<223> n = A,T,C or G

<400> 632

tttggngggc	ggngctcat	ttgggtggac	tttttgggtc	gtaggaacct	ggtatgaggg	60
gtgttttgag	tttcttcttc	gtcgtctctg	ggaggttcgg	tttcgattga	gattcgggtt	120
cgtctttatc	ttacgaggca	ccctgatatt	gttgcgcttt	ggtttggttg	tggagagttt	180
tgtctacttc	tagcgggtca	tgcggtgat	atgtagcctg	cgtggcctga	tagtgatgtt	240
gtgagcttga	gaggggagtt	gtgggtgttg	cgggcggagt	aggaggggtt	ggagcaccgg	300
gattgggaga	tatagaatca	taagtgttag	gtataggtcg	attgagcgag	ttcgtggaat	360
tcgtgtggcg	atcataatta	gagtgaggat	gggctctata	tttcttagag	gacgcacggt	420
cgtgattcgg	ggtttgatgg	gtgttcttct	tgtgggcacg	attagcttgt	tcatgatggt	480
aaggaccata	ctgtttcgaa	tgaggattcg	tgtcttcgga	ttgttggtga	tattgtggnc	540
tanactatct	agtgtgaagc	ggaggtggtt	tgccgtgggt	gagtatccga	mnttcattcg	600
ganggtatgc	gtgcggagcg	gtcctttag	acattccgga	aaaatgg		647

<210> 633

<211> 630

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(630)

<223> n = A,T,C or G

<400> 633

tccttcggct	tgggtttttt	tctgaccccc	ccccccccc	ccccctcgga	aggcctctag	60
gtcctccccc	gtctctctaa	tcctcaggaa	ccgatccacc	caaccaactt	actaatgtcc	120
tacagtaaac	acccgagaat	ataaaccac	acctaggcct	ccaatcctac	caggggaagca	180
agaagccgta	gtctagcgta	ttacgaaccc	gagatagaga	cggagatact	tagttttatt	240
ctctcggaat	aggaaagacg	actggggagg	gaatatagc	tagcgcgggg	ataggggcta	300
tggcggatat	gggggcgggt	cgctctctta	ttcttctata	ccacgtcaat	aggaatgtag	360
atatacctag	atgttcccg	agaaagagac	gttagaggtc	tccgaagcta	taaaggagag	420
gcgcaagaa	acttcgtact	ctagctttat	ataggtagtc	gctctagtcc	cataagcgac	480
gagagatcta	ctagatttcg	gtatcgccgt	cgtatgtatt	cgaaatagtc	ttcttccct	540
tttcgatctc	ctctctatac	tacatggnga	ttatagtcnt	aagatagtc	ggatattagg	600
atattagtta	tatgacgttc	gacgggacgg				630

225

<210> 634  
 <211> 647  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(647)  
 <223> n = A,T,C or G

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<400> 634
ccntcggcctt ggggtttttt ctgaccccc ccccccccc cctccactaa gancttaacc      60
caaccctata gtttactcgt ataggggaat cgaggagaaa taggaacgaa gagcgggtga      120
taaagagaaa gtactttcct ttatatgtta agagcttagc gtaatgactt tcgttatatg      180
gctagtgtgat tttatccggc gttatagggc ttagttctgg ttatctcggg tctaattccc      240
ttagtatgct cgggagtta acgagggtcac gggatagcgc gtaccctttc taaggttctt      300
ggaaagctat tcgttattta tcgcgattct cgaggtcgaa aggatcaagg atcttccctt      360
ttactaccct agtcgggtta gcggtcggtc aaaactagt tagtaccttt acctcctcga      420
aagttatagt cgaaacaacg tattagtcga aattatagcg gatagatcga gacggttctt      480
tctcgggttc tcagccggtg atccctctat ttgggggtct tctccctctt cccctttgtc      540
ttcgccttta gcttccaagg ttcctcggaa gcgaggggtt ctacttaagt cgntagcgtt      600
cctataaac cncctacagg cagaccccct tgtaaacggc tcggggt      647
  
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<210> 635  
 <211> 645  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(645)  
 <223> n = A,T,C or G

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<400> 635
ccttcggcctt ggggtttttt ctgaccccc ccccccccc cccgaaactc gccttaccct      60
agatacccaa agaatagtct cactcaactt cgtctaagta aaactctaga acttccaaac      120
ataaaagact tcgcgcggtt agctacacag cctacgggaa tctcacgaat cccgattcaa      180
gtcccactct cgaccacacc ccggtatcgt cgttttccca taccaatgtc gaaaaataaa      240
ataaaatcca gtcaagcccc acggttaagcg ggggtagggc taggcgaaga ggcaggaacc      300
gttcgaggcc gggggctttc aaaatacaaa acaactactt aaagtttacc ctttctaaag      360
tcgggggcaa cgggttaaag acgcctctaa agtactactc gtttcgagaa ggggtagtca      420
tctcccgcat agagactctc gcgtatatca actcgcacgc cttctagcat tccgacggtc      480
gcccgcggct acatatcttg cggattagct ccgagggact atagggttaa ttagtctagt      540
aaattctctt agaggatagt cggggtcgta gtttaggcagt acgaggggac atggnctgct      600
tcgtgctcta ccttgacagc atactcttat aaacatcttt ttctt      645
  
```

<210> 636  
 <211> 643  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(643)  
 <223> n = A,T,C or G

<400> 636



226

```

ccttcggctt gggttttttt ctgaccccc ccccccccc cctacgggaa aacaatcccc    60
accgagattt tattaatcgt aaaactcgcc ttccgtacca agtcttcctc cttcccgtaa    120
cctggctccc tcctagnngc tttacgaacg tccctcctct tcttacggct cggaagtggg    180
tacggtttaa tccggaggng gggctaacga atccaaggct aactcctctt anagtttggt    240
gtccnncnct ttagtaagga tccgtggagg gcgagtattt gnccccggc ctttattnta    300
tagttcccta gtacgataaa gntaccggct atcctattac agcggataaa agttatttan    360
agggccgacg tcnccgctag acaggctaca gctagnngag gtaccgcctc cgactantcc    420
gttgnttcog acaaggcnagt ttcggttaac tccacaaact cctccgccga ctctanggtg    480
gggacggcag ttccnncggt tagtgtgcgt tatagagaag ggcatttgag ttggacgtta    540
cnttttaaca taggttattc cgtttagggt cttgcgggcc cgtgggggta gtnccnccggc    600
gcgttnntat cggcgatttt ccgcagtttc cgtttccggn tnt                               643

```

&lt;210&gt; 637

&lt;211&gt; 631

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(631)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 637

```

gggtntctc atttgggtgg actttttggg tcgtaggaac cggtatgnag gagtaggagt    60
cgctgggaag actagaagtt agctacggac gattagtgtg attccactct taataacgag    120
taatcgttta cgtcgggttg gtgtttcggg gttttggaga gtaagcgtag ttgtggagtt    180
tcgcatatag gtccccctac ttcggcgatc tcgtcttctg tcggttaggt tattattggt    240
catccttcgc attagtagta gggtttggtc gataaatcga tagctattct ttagaattcg    300
tagtcggaga attcgtgtac gaagtccttt aagttcttta agttcgcgag taagacgtgt    360
acgggttatt tgcgtcgac gtaggtgtcg ttacggggag ttctgtttta ggggtttacg    420
tagaacgtta ttaagcacgg taatacgata gaggattacg cgacgtattc gtcttagaac    480
gtcgattttt cgaagggcga tttgttatcg aaggggagtc cttggagaat cgagatattc    540
caagaatatt acggagatta cagatcggaa ggctcccag atcggacgta ttaccggtct    600
cgccccgaac gagtaggtat cntccggata a                               631

```

&lt;210&gt; 638

&lt;211&gt; 606

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(606)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 638

```

ccccccccc ctcaaccatc nattccccac ctcaacgcga attacggttt cgaaagtcga    60
caataagtcc ggtcgagtag agggaatcag gggctggtan aaaggaccac gggcggaaaa    120
taccggtctc cttccgggga gcgacgtcgg ggaagggaag gagagcggtc tagttcgtag    180
gcaaacaggt cagaaaagtt aaggttaaag gtcggagggg agaggatagc tagtacgctt    240
agttcggggc tcgggcgcag ggccactttc ctctttcgcg ttcctttact ctgcttacga    300
gttcaggctc cggagttccg cgccggaggt cgctcgcgac ctagggaatg ggactcgctc    360
agtccccggt tatccttcgg gattctatgt tttcgcgat agacggagac cgggtagtag    420
ggttccgctc taccgccact cgtcgccttg atccggcccg ctccgcttaa gggcgatgaa    480
agattaggtt ttagggctct acgggacgag gcatagggcg ggagaagggg ggaggggctc    540
ggggtcgaag ggantaagaa atcgcantcg cgcggggtcg gtagganccg aaatttttct    600
cnncgt

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227

<210> 639  
 <211> 592  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(592)  
 <223> n = A,T,C or G

<400> 639  
 tcnttcggct tgggtttttt tctgagcccc ccccccccc cccccgggaa cgagaaaaca 60  
 atccccacct accgcgggga gtgggtttna cgcttagttc tagaatcctc ggaatcgtcc 120  
 tccggcggttg gtagttccgg cgattccgag tatgccgaag tgtatcgctc cgtctagagg 180  
 ttggtatctg tttatcgaga tgacgctatt gactcggatg ctttcgaagt agggggatag 240  
 gcgcatagat acgcctccgc ggtgtcctct gaagtggccg catccgtgga cgcagcgtag 300  
 acagctctgg tggacgataa cggcttctcg tactcctact ccggctatta tgtagagag 360  
 gacttggttc tgaacggata taccattagc gaaggggtac cctccgctaa cgcaggcgtt 420  
 tctaacagtt cttccgggcg ctccgaattt agattgacgc ctccgcagca ttgtgggatc 480  
 ctcttcggtt agccctcttt ataggatttc tcctccgcc cgaagangg ctggtcgtcc 540  
 ccggcangta tgtctagctc gaacgctttg ttactccttt gttttcgaaa na 592

<210> 640  
 <211> 637  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(637)  
 <223> n = A,T,C or G

<400> 640  
 ctttgtggcg gtgntgtct catttgggtg gactttttgg gtcgtaggct tatccgggtn 60  
 gggctcccga agtagcttag gatcgccggc tagttccggt cccgcccgtc gaaagcgcg 120  
 ttccggcgggc ggcccccgct tcgttcgagg gctttaccct catagagtgc caggctcgg 180  
 ttcttacggg ttccgctggc atagatttta cggcgagagg tcggtatctt cgcgcgttta 240  
 cgttcgggtcg gcatctacgc ctagtccaca ggtagtttat gcgccggagc gcgtagcgga 300  
 gaggttatac gggacgcgga agaaccgcct ccaaatgact agtacaggct cgttcggggc 360  
 tagatctcct cgtcgggtcg gcggttctta cttctagggc cgctctacgg ttaaggcgg 420  
 tcgtagatc ttagaaacta tactcaagtt tcagtcggaa gaaaggaggt agagagaagg 480  
 gtaaacgatt acctccggtt ctagcccttt ttactcgcat aacgggagaa cggggtccgg 540  
 ctctcagata cgcctcgga gacgtcgga ttcaacttta acctccgcta gggcatccgt 600  
 atacggttaa cgcggtaaaa gcgacctcgg aaacctc 637

<210> 641  
 <211> 649  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(649)  
 <223> n = A,T,C or G

<400> 641  
 ctntgtggcg gtggttgtct cagtttgggt ggatttttgg gtcgtaggna acctggtatg 60  
 aggtctagtt tcttcaacga ttcttggttc agttacgga ccctatcctt atcttacaat 120

228

```

gtcttctaca tcaggttcat caattaatat atcaattaca cattaacgac ggtgtgacgc 180
aatatgagaa agtatacatt aaggttatta tatattattc gcttaaaaag gttcctgaca 240
tgggacaact tcaccacca ttctagaagc ccccccctct gtaggacccc ctcgagtcc 300
ccattatctt agttcagttt tcatttttta accaggaggg tatcggtttt taataggtac 360
tattttgtca aacttttcag aagctttatc ttcaaatata cttgcaccat ctgtactagg 420
agcactaact attcgagtct attacagctc aacagaaaat aattgaaatt aaacaaccta 480
agtatcgccc accataaccc catcgggctc tcacccatt tcttcataag ttctagagca 540
tcctgagctc ttctctatta cccttgatgg tactcatggg ctaatacccc ccgcagttat 600
aggtccttat ggatcctatg ctaccaccgg tctaattccct tctatcacn 649

```

<210> 642  
 <211> 645  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(645)  
 <223> n = A,T,C or G

```

<400> 642
tccttcggct tgggtttttt ttcgtcgcg gttactatta tcgattgtta cttgtaaagg 60
cgatactccc accgctcacg atattagacc tgctcctcta gaagcgacg gcgataggct 120
tactcgcccg gcgaagacgg cgaacgggta ggaggagcca tatgcaaccc taacggagat 180
tataagtact gggaaaaata ctagtattaa ggtagcgggt taagataggg ggagagacac 240
tattcacgag cataagcact tagaagggtc tctcgaggag aggtaggcta cggactacgt 300
tccttcttcc tctagcctcg agaggagta tagatgatte gcaaaagaga atccctccta 360
tacgctggca taactagacg acgcgtcgtc gggaaatctc gccaaccccta ttgcgacctc 420
caaaaggaag attgtcgttt catagaacgc taatactccg ggtcttcccg aatcatagcc 480
gcatacgggt aagaagacgg taaaatcgcg cgattctaac aagattctgt agacttaagg 540
ctaagcacta gaagcgatct cgattccgga tcttaagatc atactaatag ttcggtcaca 600
ccagacgacg attagccact agaagcccta ctccgtngaa accgg 645

```

<210> 643  
 <211> 586  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(586)  
 <223> n = A,T,C or G

```

<400> 643
ctttgtggcg gcggtgtctc atttgggtgg atttttgggt cgtaggaacc tggtagcag 60
ggtccgcccc gaattaaaag cgggatcccc aaaacgnngn ttcgcaagaa gagaagaatc 120
atagcgatag anctttcata gtacaaaggt aactaagagg aaaataatgc agattcagaa 180
ctagttgcc aattagaact cgattaggcc aaggatccga gcctggcgct atcacttcgg 240
gacttaagct acggtagacg agtcggtcct gaagcatagc tcccgtagga cgtaggaaac 300
tagtccggca cggaggacat actctcgagt ctcggaacgt ctatttagaa tataaacgca 360
ttaacctcag aagcgccga cgcggttact ctctagggaa ctatttcatt cttccggag 420
ctcccctatt ttccaacac atataccggc aaaggaaaat cttntgtcct cggctctaaag 480
agagggaana aaaacgatat ctagggtcgg gtttatccat taaaaaanat ngacgcgact 540
actcccttcc aaagggtgtt tcccctagg nagagttcaa cnagaag 586

```

<210> 644  
 <211> 646  
 <212> DNA

229

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(646)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 644

ctttgtggcg	gtggttgtct	catttgggtg	gcatttttgg	gtcgtaggaa	cctggtatng	60
agggctattt	gacttgtttc	tcaaattcca	tggtatggtg	ggtggcgtgc	ggggtggcgg	120
tcggttcggc	gggggtgggg	gtcgtcctcc	aaaggagtgt	ctagagggct	tttagtggtt	180
ttagggcggg	aaggggttag	agcggagaga	cgtcgtcgtg	gaagcttctg	gcggagcggg	240
agaaggtagt	tagcgcgggt	tcggaagatt	ctcagaattc	gagaagaggt	agtggggcgc	300
ggagagagag	tttctaagtc	taaacgtaga	ggtcgtccta	gtcgggccgg	gagtagcttt	360
taagctagag	gtcgaaggtcc	tcgtttaggc	tccgggctct	tcgggcagta	tcctctttct	420
cgaaggaacg	agcgaccgac	gtcgtagccg	gacccgtcta	tccgtacgtt	tagagatacg	480
ctcacctcca	cgggcgtata	tgcccgtata	cgtataaacg	cgtaatatatac	tcgcgcgtaa	540
aacacgtata	cactatatac	acgcacgtga	cggaccgtat	agcgttatatac	gcgcgcgtat	600
attaatttac	acttatatac	gcgttaaacac	gatatatcac	acnccg		646

&lt;210&gt; 645

&lt;211&gt; 654

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(654)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 645

nccttcggct	tgggtttttt	tctgaccccc	ccccccccc	cccccggtcg	acaacgtgcc	60
caccgttgcc	atcccagcat	agctggttcg	ttctgtttta	ttcttagtag	tttagttcgc	120
ctatagtccc	tcgtctatcg	tctatcattt	aaggaggcgg	ggctcgctct	ttagggcggg	180
tatcttaggt	attcttcttg	tttcggctgc	cgtctcggag	tctggtcctt	ttgctttcct	240
ttcttggtcg	aacttcgtgt	ttgatcgcgt	tgtttctttg	gggtcgtcat	acctaagggc	300
cacttcgccca	acaaacaagt	ttgtgtagtc	gtttctatta	gggttcgctg	gccggcgctc	360
ttactggttg	gcgattttta	acgcgttttg	ttttaatttg	cttcctcccc	tagggctcgc	420
tcggtcttct	ctctgttcgc	tgctctcgtc	cggccttttg	tgccggggata	gctccggcta	480
ttancgtgcc	gtgtccgtgt	ggnntttgtc	caatgtgaag	gcctaggggt	gcgggcttct	540
ttggccatgg	nttccctct	tgtgancctt	aggggtaacg	antcgttaatt	naaggtcggg	600
ggttggnata	cgttntangg	gangcctgng	tccgntatct	cttgtttttg	cctn	654

&lt;210&gt; 646

&lt;211&gt; 645

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(645)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 646

tccttcggct	tgggtttttt	tctgagcccc	ccccccccc	ccccacgcc	aagtacacag	60
acccaccaaa	aacaacgtca	acacaacttc	gggtatacgg	accttaagag	agaccccgta	120
gtagacccta	ccacagccat	ccaatagtca	aacaacaagg	gcgcacccaa	tccatccata	180
gagctatcaa	acaacggagg	ggaaaggaaa	gagcagggtc	aacttagcag	agatcgaagt	240

cggcactaat	tcctttcaag	tactcgctcg	gcttgtagtt	cggggtaaag	tccgctctca	300
aaggggccaac	gagggttttaa	agcgaccccc	gtatcgagtc	ttcttcgtat	tcattaaggc	360
gttaaaggta	cgagacctag	aagagagtag	aattagccca	ccaaatcgcc	taaaccggca	420
aaaacgacca	aaagtcaaag	acccttacaa	atatacctt	aaaacgcaa	ccccaaaaac	480
gcgatcagta	acgcacgtac	ctttccacg	cttttcttc	tttactctc	caaaacaaac	540
ccgaatattt	agcgcaaaaa	atatccgagg	gagaattaga	agctattacc	cgaaaaaaa	600
ncgganang	antaaatngt	ggggaatana	cgtttggtt	ttctg		645

&lt;210&gt; 647

&lt;211&gt; 753

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(753)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 647

accttacctg	gtaccgggccc	ccccctcgag	ttttttttt	tccaaataca	actcagattg	60
tatacgaaaa	gctgataata	cattgacttt	tgtgttttaa	atcccttgag	cctttgataa	120
tgattttttt	tgtgttaaca	attgtagtat	ataaaatcgg	attcaccatc	cttctgatgc	180
catattgatt	agtttgattt	tatggtgatg	ggatcattgt	gtgttaactg	tattaagaag	240
aaatggattt	gattgacttt	gcattccattt	ttatctgtgt	tactttcatg	ttttatttaa	300
aagcatttct	ggaccagaat	aagttaagtg	gtataatttg	ctttttacac	gtttatataa	360
ttgaagttag	caatgtggca	aaatctctaa	tggaaataaa	atgcttcaga	atgatgacat	420
aaatctgagc	tatttcttgc	ctggagaaca	agtgttatc	ataataattt	aatagcttct	480
gaggtgtttt	gttcacgtga	tgaaggctta	tccaccttgt	atcaattcat	gggctctgct	540
ttgtttaatg	tagtcagggt	gttaatacna	gacttaagag	tcctcctact	gtgataagtg	600
gtgagtgaag	attacatgtc	ttangaaaa	tatactggga	atatctctga	cattaatggg	660
tttaaatgtt	ttaaggctag	gggatgatgc	aatgganaan	atncttccaa	angtttctgg	720
ttgtttatat	ttgnngaagn	catnaagana	ccg			753

&lt;210&gt; 648

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 648

gatatcccgg	ggaaatgcgg	aggcctttng	gcttacgtgt	ttaccgcgta	gggcaaagcc	60
ttgncaaatt	cccggccagc	ggagcggcga	gggtggggac	tcacgggaag	ttaaacagcc	120
tcgtcggcgt	cctcgaggct	ccaaaaccag	gctctaggcg	gggacgactg	cagccgttat	180
ggaggccacc	gcggctacgg	ccgcggctga	ggcctcccca	ggtggagcgg	tggcctggag	240
gggaatcttg	atcctggggc	agccacctgt	caagaggagg	cggagcgtca	tgcctctgga	300
agactggatg	aatattctcc	aggagcctga	cgaaggcgaa	gaagtctttg	cagaggaaat	360
tgaatgctgt	ctgatgctac	aat				383

&lt;210&gt; 649

&lt;211&gt; 349

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

231

<221> misc\_feature  
 <222> (1)...(349)  
 <223> n = A,T,C or G

<400> 649  
 cgattgtnta cnagtcttag agtaagctta agntcgn tac cgagctcgga tccactagtc 60  
 cagtgtggtg ggaattccat tgtgttgggt cactagtaaa tggatttagc tagacanagg 120  
 anatttaccc tattccattt agcacagtga gganaggcta nacagctagg atgcaataaa 180  
 aaaaatttta atgagaaatg tgtgtggttag attaatctta ttaatctcaa gttatagatt 240  
 aaaaatttta agtaccncat aaatgccatt tgcctttgct aangntacat ttttatgaan 300  
 aangaccntg catacnaat ganatactgg actttnggna cttgangga 349

<210> 650  
 <211> 306  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(306)  
 <223> n = A,T,C or G

<400> 650  
 cattgtgttg ggagcatcct tccatcagct cccatgagaa attctctgtt gggtttaagc 60  
 aatccccaaa tatatcatat tgacatgaat atatcatctc ctcaatgtcc agcattagca 120  
 gacaagatga gtgtcgaaga tgatataact cctacctctt atgtaggcta gaggtaaagt 180  
 ctggctctgc tgactgtggg gacataccga aaaggaatgt gggttaatat cagangacct 240  
 cctgcagat ccganantca gggncctggac tttctgggan aggaagcnaa aagttatntc 300  
 tgaacc 306

<210> 651  
 <211> 769  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(769)  
 <223> n = A,T,C or G

<400> 651  
 cattgtgttg ggcagggtca tttctaaggc atgggctgga agcttttatt taaaacttta 60  
 catgtcttag aagcactctg gttgttgcta ggcagacaat ttacatctc ttgctatacc 120  
 agttgcatga agttcatcat gcatattggc tgtggaaaac cttaacagca tcatgtcata 180  
 aggtttcagt aaggtttaaa tgaaatcatg tattaagcac ttagtatagt gcaccttaaa 240  
 tgttagcttc aaaacaatga caacctaaact aatgttgaaa gaagcttggtg tttgtaaatt 300  
 atgtcttatt gaaagatgtc atcaaactct gttatttcta atcccttaaa gtctctcaat 360  
 gtatttcttt ttgccatata caatgacagg acctagtgtt aagccagtgg ttctctcaac 420  
 ttctaatacca gagataacct ggtgtcccca agaccttttc agagcatcct tgatgtcaaa 480  
 accattttca taataatatt aaaatattat ttgctcattg tactcttatt ctctcccaaa 540  
 tattcagcga gttttccaga agctatataa catgtggtaa catcttatca ctctgacgat 600  
 taatagaata tgnngttttg gattcttgng tttaaaattt tctcactttg gggttctaatt 660  
 atggnnacga ttaatagata tggncatccat gaccagangg ctttaaagca ntcaataatt 720  
 ttttaagagac taagnactat cttttaaaga tngngaactc catcttaatt 769

<210> 652  
 <211> 267  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(267)

<223> n = A,T,C or G

<400> 652

nnangccctt	taaccattgn	ggcctccacg	cnntggcgcc	cgctctacaa	ctagnggatc	60
cgcnactcta	gnanaangat	tggctcttnt	gggntgggcc	ggncgggctg	gggcgttaag	120
cggggctggg	cgcgcgccgn	ggttgnaacna	ggcgccgccc	ccncacacn	cccggagcac	180
cctntttgcn	gcctntcccc	gtcaccccc	cgcgcgccgn	tccgcttttt	ccncacccan	240
agcncntttt	atctntgtct	cctccgg				267

<210> 653

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 653

cccnttnacc	cattgctgga	ctccaccgcg	gtggcgggccg	ctctanaact	agtgggatcc	60
ttncnatgag	atgnngcgang	gaggacnnat	ttgctatnct	ggatggggct	gantcntnta	120
gctnctctag	cancagatgg	gttatcgagg	aagatgactc	caangggcta	nantcctatg	180
cncatcctaa	aanncanctg	ctgtnttcag	agtacgcgac	acatcatcnc	tnatgcattg	240
ntgancaaga	cgggcangtg	cttatcctca	gcgangatgc	ccttaaccan	gagctcgaat	300
ggacntatca	ccntanaggt	acanntnccg	caccacacac	cngcttgcn	cctgacgctg	360
gactggatcn	cttaggccac	caatnccccg	tttnccacat	ncctgggacn	ctananatac	420
tcganggggg	gcccgttanc	caattcgccc	taatactgag	ccttgntacg	nacgctnact	480
ngngtccta	ttanaacggt	g				501

<210> 654

<211> 710

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(710)

<223> n = A,T,C or G

<400> 654

gcgnctttan	cncatgctgg	gtccacgcg	gtggcgggccg	ctctacacta	gtggatccca	60
acactgagtc	caccacagna	aaactcanca	ccaggcagac	cccacaactg	cagaatccag	120
gctgcaattc	acagactaat	cntctagacc	cacctcagta	ccagatggta	ccacacagct	180
caaggnttta	ggtttgctg	gtanactcaa	tctctatctt	tcaccaactgc	cagcctgact	240
tcagagatcc	tgngctctgg	acagtctca	gtggcaggca	actctcagga	gcctcaggnt	300
tttggcacat	cccagnacca	gccagctgcc	acaggccctg	accttntanc	aacactgccc	360
atgtattcca	gacttctanc	ataccacagt	gccatgctga	ttgcatctat	agangctcag	420
gtgcncctca	aanctgtgcc	tgctgcagna	ngccccacgt	ctctggcatg	ccccaatgcc	480
atngtgggna	acanttgact	tctgggcatg	ntgggaattcc	ctaccactga	ncctgaccat	540
aggngggganc	ccattttttt	cgaggggggg	gccccggccc	caattccncc	ntatagnagag	600
ncgtanttac	gcgcnnctta	ctnggccngt	ngtttaacaa	cgtcnntgan	ctgggggaaaa	660
cccctgggng	cnaccacaaat	taaacngcnt	tgcannacat	ccccctttcg		710

233

<210> 655  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(202)  
 <223> n = A,T,C or G

<400> 655	
ccccttttccc ctttcacccc ccccgttttg gcngccgcgc acacctactn catccaccca	60
cantcgacca cccgagcttt tttccgatcc cancatcnat gcngattttt tctntgcntg	120
ctgngcctgc acctttgnta ggtcaagcct ggcccatctt cgacaacttc ctcacacca	180
acgatgaggc atactctgac ga	202

<210> 656  
 <211> 308  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(308)  
 <223> n = A,T,C or G

<400> 656	
gctgntgaaa gaccacaccg aaaaactctn ctttccgact tccacatgat gatcngcatg	60
tggtggtgag agacttatca tgacgacatc gcttccnacc atcgcanccn ctgcccagc	120
ccattcatgg aggcctgggn anttctgtga ntgacntnga cnctanacnc tnccactgtn	180
tgtatccag acttgnttng aatatnttat tggcnaaana canttncgga atgctgtgnt	240
tguncattga angatctgat cactatgaga gggtaggagc nncctgctng ctggcantnt	300
ntaacccn	308

<210> 657  
 <211> 696  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(696)  
 <223> n = A,T,C or G

<400> 657	
accntttcca caatnctgmn ctccccgcgg tggcgccgcg gtcgaccagc aacctcagct	60
gtgggtcttg ttacagtaat gagttactgt aaggaaagtg tgacatttcg agcaatttga	120
tttgtttaaa aactagagca gtttcagggt tttccttgta aatctgtctt atgtgtcttc	180
aatgttcttt cttgaggagt agagaaagga attgtagga atgatgcata aacctaggct	240
tattttatct cgctgccacc cataatcaga gcagattctt gggactatga cctcatgga	300
gacatgacaa ttgtgtgtgt ggtgggtggg agaaaagagc tgggaatttt tagggcttag	360
agggtccaat caggactatt ttatggagct ctgctcacca actttaagtg agcaccaggg	420
gtngaaagc gaatcttggg ntcaaaaana caatggnaag gggtaagtgt gtatnctgaa	480
ctggccactt cggactctta ttaactggg tattctcant taaggaggcn nggggtgtct	540
tggcttgtna aggaaagcct gtgcaatgga atgactttta aaccccccat taaaaaaa	600
angntataaa tcttgggtct taanaangaa gcctgggttc tnttanccca ttttcccc	660
gggaaggnaa atnttcttag gnaangaa ggaagg	696



234

<210> 658  
 <211> 698  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(698)  
 <223> n = A,T,C or G

```

<400> 658
ctggactccc cgcggtggcg gccgctctag aactagtgga tccgtgttgg ctcaattctc      60
aaggctgttg ctgtgcggcc tgttccccac acgtgctgct cagctcaggc aagcaccgag      120
cttgtgttgt ttcattgctca gcgtggaggc ccctcctcca ggtcgtgct ctgtggggtt      180
ccatacact caggctccta ggaggagtcc atttagaaag ccagggtttt tctcagagtc      240
ttagttcctt gtgctgtcat ccatttcaca cgacttgggc cctgctcggg gcaacacagc      300
aagagaaaaa acagggaaaa taagagaggg accttgacaca cacacgctct ggaccacaga      360
gccctgtgcc cagctcctct gtcaatacag gtggaatctc gtgcaggatc gcagggggtc      420
gtgatgccac caaagagcag gccgggacag ggtaggaga gaaaggagag ggaagtgggg      480
gtttctccta cgcactotta ttgacagagg gaaaggcggg tttgtattgg ggttgtcggg      540
ctttgcaccc acngcacagt tgtgagacac ccccatcctn agatcaaagc cccacataca      600
gcttggggaa aaacaaaacn aaacaaaaca aaaacagtaa acctccatgc canttgttgg      660
gnaagttttn aatttncttc ccnaccan cttgtctc      698

```

<210> 659  
 <211> 750  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(750)  
 <223> n = A,T,C or G

```

<400> 659
ncaanctggn ctccaccgcg gtggcgcccg ctctagacta gtggatcctc ctcatgggcc      60
tgatattctc tgaacatatg atgaacattg cttatgaaaa attatttgta ngaaaattgt      120
gaggcctaag aatgntatatt tcttttagtg atggctcttg tttgcttctg taaggnaactt      180
gtgggcactc gtaagcttgg atctctttaa tctaatacca gntttgagat tttcttggcc      240
ccatagatga attaaaactg gcgtacttct tgtttacaag anggataagt ctcctagggt      300
aagtcctttt ggggtcccaag tcaaaaagat gagggattta ccagttctct aaccttggtg      360
gccccagact ccaaactttg ccttctagtc ccaagaggct atcaaaaagc aaaggccatc      420
ttccaccttc ttttccanaa cagcacacat tccagacagt acttgaaagc aggaacctcc      480
ttatccctta aaaacctctt ggaancatct tccctctctt gcttctacta tgcttggccc      540
acctancatt cncntttttc tggaaaaccg gaaaaanctn tgactnnngt tggctacatt      600
cagcttggcc ccctacaatn tggtttccat ctgccctaan gaaattttta agggcacttt      660
ttttntggcc cctgactttc nntttttagg gctttccccc angetttgcc cctttggtta      720
aaggggttat tttccttccc cttttggaag      750

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<210> 660  
 <211> 849  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(849)

<223> n = A,T,C or G

<400> 660

tcggatccac	tagtccagt	tggtggaatt	cgcgcccg	gtcgacggc	agtagtgga	60
tgcntntcta	aatgttataa	ttatttcaga	attactctgc	cagaaagta	tgatcatata	120
tagaagagtt	tgtagctaac	tttgaaagta	gtggaaagtg	gttttcagt	attgtttggg	180
ttaatttaaat	tttgattata	tttggttttt	agttcaggta	atTTTTTgt	tgaaaacttc	240
aaatgacaat	ttcttcattg	ttactaaaga	tcactcatgt	ggagtagttt	cagatttttt	300
tctgaatata	tgtattactt	ttagagatgt	aaagatgtga	aattactaag	agagaaaccc	360
atgtgatttg	tttagtggtg	caaaagtcgg	tagctccttt	gatcctaagt	gccactgata	420
gttaaataga	tactgaagct	atgggcaggc	tggttgata	agaaaaagg	agacagagaa	480
atgggaaatt	gggaaagaac	tgtgcaaata	ggaaaaggag	agagcaacag	aacagaatta	540
gtaccacagt	gccgaagtgc	cacctcaggt	acttccatct	cccatctcct	gaagaattca	600
gtaacagttt	gcaaatgggc	aacacaatca	tttagtgatc	ctggttgata	ttttcaatac	660
tttctgggga	tttcttggct	ggnttcaaaa	gatgatctg	atagttttat	tgccctgaa	720
ggtattctga	agnttancat	aattttattg	tcagtaaaat	atTTgaataa	aagngganga	780
aggaaaatct	ggcntcttat	tttgggatnt	cngcnggggg	aangaggata	taattnaccc	840
cggccttg						849

<210> 661

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 661

aacttaagct	tggtaccgag	ctcgatccc	tagtccagt	tggtggaatt	cgcgcccg	60
tcgacctcca	ttcgtttctt	gtcctttttt	ttcatttttt	ctcatgttct	attcacttta	120
ggtttctaag	ataaatatta	taaaataatt	tttacttata	aattattcac	tgataccctg	180
tctttaacat	gtgaaatgaa	ttcaaaagga	atcttaatga	gaaataatat	actcatgatg	240
tttaatagat	ttgatttcga	aataataagc	cctctgaagt	cctaagttaa	aaataaagca	300
acttggttga	taatttttca	tcaagaatgt	atctgagtct	ctgagtaatt	attagtagga	360
atattccatt	atcacaaatta	cacagtataa	gctattttagt	ctaactttac	caaaaaagg	420
agctacttca	acactgtgtg	agacttttaa	ttgggttgca	ttgggtatgc	actattagca	480
agataaccta	ttttacagca	gtgtttntta	acctttccca	tttatttgaa	aggcagctaa	540
gataatagtag	ttaatntaan	gggctgatgc	atTTtatatta	catgtagana	atgggagata	600
cnaaaggag	nggggggana	tnttttgnat	tcnnaagctt	cnttgncaat	taa	653

<210> 662

<211> 646

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 662

aaacttaagc	ttggtacccg	agctcggatc	cctagtcag	tgtggtggaa	ttcgcgccg	60
cgtcgaccga	gggacaggca	gccagngctg	gggtcaccag	ggtccctct	tgggccctcc	120
aanagcaaca	gtactggcaa	cagctgggat	ttgctgagca	cagactctgc	agcaggctcg	180
gttgagctct	ctgtgcctgt	tccttcatac	catcctcacg	cccatccatg	agatgggtcc	240
agctgttttc	agatgagaaa	atggcacagg	aagctggtaa	gtgacagtca	gaaatgaatg	300

236

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ctggcagctt antccttga cccaccgag tgcaggacct tgctcaacag ggatcacccct 360
tgtccgccac ctgttcatga ggccaccag ggtttgtgtg gtcatttgtc tcctttcatc 420
tgcttgccct caaccagctg ggtcattagg gctggggaac ccagacccca cacagtcctt 480
ctcccagang ccagacacan notncgccac agnaaggact tcagtcctccg aancaaatgt 540
ncctgggcgt anaaactgna gggnccccaa tccctggtgg ggtactgctt tgcactggng 600
gaattcaccc ctcattgnna acctttccct nttncaccc ctaaac 646

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&lt;210&gt; 663

&lt;211&gt; 650

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(650)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 663

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aacttaagct tggtagccga gctcgatcc ctagtccagt gtggtggaat tcgcgccgc 60
gtcgacgtcg acgcggcgng ccgtttcgac gcagttgata catattatta tatactacat 120
nggttttcta gaattaaaaa attaatgtgt agtgccagcc ctatagtgaa gttacatata 180
tcaactctat ccaattttgt cagccataaa acttaccttt ttcacatact tctaactcta 240
acaatgtgag aaatgtagat cattgcaatt ataccacaa ggcagatggc tacatgcaga 300
atggatagca gaatctagct acttacgcta gccacatggt agacgttttt tcctttgttt 360
ttgcaaaatt gcaatataag ttgcatatcg ttagagttaa aagatgtaa gaaccatag 420
aagccagtga tgaaggacat ttatatattc acctttacaa angaccttaa aattgcctat 480
gtggagcaga aactggagga gggcnaance atcngtaaaa aaaattttgn tncattttgg 540
atttgggcac cattattacc tccccaggtt cctttttgnt ttaacctttc ttttaaaaaa 600
aataattcnt aatttttggg caaaaaaaaa caagggtttt attfaaattt 650

```

&lt;210&gt; 664

&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(678)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 664

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taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt 60
actcatcana gctaaatgag agcgctttta aaatgttagt ttgtcttcg ccattttctac 120
agaaagctgc aatttcaggt tttcaacctt ataggtgata ttttaagaaa aaaaaaagca 180
atcgcaaata gccccactgc ttttacaatt cattttttct cttctaggta tagcctgtca 240
ggtggcctaa tgtaattttt gacatctcta ggaattttta tagaaccaga aatgggtgcc 300
agagatatgc ctgcactaat cttaagtggg gatttatgta tttctcaagc aagtgattaa 360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt 420
anaattatct taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata 480
aaaaccacaa aaggtcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga 540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct 600
attgggcata aaatagacca aagaccagtg ggaacacaga taaagaancc caaaataaat 660
cctatatatta cngccnc 678

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&lt;210&gt; 665

&lt;211&gt; 694

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(694)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 665

cttttcaaat	catttttinct	cttctaggta	tancctgtca	ggtggcctaa	tgtaattttt	60
gacatctcta	ngaattttta	tagaaccaga	aatgggtgcc	agagatatgc	ctgcactaat	120
cttaagtggg	gatttatgta	tttctcaagc	aagtgattaa	agcaaaacta	ggcacgattg	180
aaatcaagat	cttttaggca	anaaagtcac	gatgagtttt	agaattattt	taggactctg	240
tggctttctc	ttcatagaaa	tagaaaaaaa	aattgtataa	aaccacaaaa	ggtcctgaat	300
agccaaagca	acactganca	aaaagaacan	agcagggaag	caacacacta	ccngaattca	360
aattatacta	ccagggtgta	gtaaccacaaa	cagcattcta	ttggcataaa	atagacacca	420
agaccaatgg	ancagaataa	agaaccccac	aaataaatcc	atataatntac	cgccanctga	480
ttatcaataa	cnaacaccaa	gaacataatnt	taagggaacnt	nctattcaat	aantagtgtc	540
ggnaaaaact	gggaaatcca	tatgcagaaa	naatgaaact	agacccttat	ccctcaccat	600
acgcaaannt	caacttcgga	atgggattac	aaaacttaag	acattccaac	ccaagaaact	660
atnaaancta	ctattaagaa	aacagatcnc	nccc			694

&lt;210&gt; 666

&lt;211&gt; 705

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(705)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 666

tttaaaaatt	tagatacact	angaaaatta	ttttagtatc	agaagaatat	caggggggtgt	60
agtactcatc	agagctaaat	gagagcgctt	taaaaatgtt	agtttgtctt	ccgccatttc	120
tacagaaagc	tgcaatttca	ggttttcaac	ctaataagggt	atatttaaga	aaaaaaaaaa	180
gcaatcgcaa	atagcccccac	tgctttttaca	aatcattttt	tctcttctag	gtatagcctg	240
tcagggtggc	taatgtaatt	tttgacatct	ctaggaattt	taatagaacc	agaaatgggt	300
gccagagata	tgctgcact	aatcttaagt	ggggatttat	gtatttctca	agcaagtgat	360
taaagcaaaa	ctaggcacga	ttgaaatcaa	gatcttttag	gcaagaaagt	catgatgagt	420
tttanaatta	ttttaggact	ctgtggcttt	ctcttcatag	aaatagaaaa	aaaaattgta	480
taaaaccaca	aaaggtcctg	aatagcccaa	gcaacactga	acaaaaagaa	caaagcagga	540
agcaacacac	taccagaatt	caaattatac	taccaagggtg	tagtaaccaa	aacagcattc	600
tattgggcnt	aaaatagacc	naagaccaat	ggaacagaat	aaagaaccca	aaataaatcc	660
atatttttac	agccagctna	ttatcaataa	aaacnccaag	aacnt		705

&lt;210&gt; 667

&lt;211&gt; 817

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(817)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 667

nnangacttt	tgtggnttta	tacaattntt	ttttctattt	ctatgaagag	aaagccacag	60
agtcttaaaa	taattctaaa	actcatcatg	actttcttgc	ctaaaagatc	ttgatttcaa	120
tcgtgcctag	ttttgcttta	atcacttgct	tgagaaatac	ataaatcccc	acttaagatt	180

238

agtgcaggca	tatctctggc	acccatttct	ggttctatta	aaattcctag	agatgtcaaa	240
aattacatta	ggccacctga	caggctatac	ctagaagaga	aaaaatgatt	tgtaaaagca	300
gtggggctat	ttgcgattgc	tttttttttt	tcttaaatat	cacctattag	gttgaaaacc	360
tgaaattgca	gctttctgta	gaaatggcgg	aagacaaact	aacattttta	aagcgctctc	420
atttagctct	gatgagtact	acacccctga	tattcttctg	atactaaaat	aattttccta	480
gtgtagtcta	aactttttta	aaaagacatg	taatccgcgg	agtttgtaac	tcaaaacgag	540
tgcatctagg	aggtatcgca	agccgtttct	ggattaaatt	cccagctagc	ttgcttgctt	600
agcaggggcg	ggnaaanaag	acatctgcag	cctagggaag	aaaacctttc	gcattgttct	660
tacgtgttta	cggtatttta	tttctanaa	caaggcngaa	ttgggactcg	aatgggtcag	720
ttgggggtgg	ggatcccctg	gtncataaaa	ngtcanaaag	anggtacagg	cggaacncca	780
agggtcgtcc	tgcatttana	ctcggaattt	tggtgcc			817

&lt;210&gt; 668

&lt;211&gt; 826

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(826)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 668

cggggggnnt	tacgtctctc	tggacgcttt	tattgtacca	gggcgatccc	agcccaactg	60
taccattcga	gtccctactc	ctgccttgct	ctagggaat	aaaataacgt	aaacacgtaa	120
gaacaatgcy	aaagcgtttt	cttccctagg	ctgcagattg	tcttcttcac	cgcccctgct	180
tagctagcta	gctagctggg	aatttaatcc	agaaacggct	tgcgatacct	cctagatgca	240
ctcgttttga	gttacaaaact	ccgcggatta	catgtctttt	taaaaaagtt	tagactacac	300
tagggaaaat	tatttttagta	tcagaagaat	atcagggggt	gtagtactca	tcagagctna	360
atgagagcgc	tttaaaaaatg	ttagtttgct	ttccgccatt	tctacagaaa	gctgcaattt	420
cagggttttca	ncctaataag	tgatatntaa	gaaaaaaaat	acaatcgcan	atagccact	480
gctttttcaa	atcatttttc	tcttctaggt	atagcctgtc	aggtggccta	atgtattttt	540
gacatctcta	ggaattttta	tagaccagaa	atgggtgcca	gagatatgcc	tgactaatc	600
tttaagtggg	atttatgtat	ttctcaanca	agtgattaaa	gcaaaactag	gcacgaatga	660
aatcaagatc	tttaggccag	aaatcatgaa	nanttttana	attattttan	gaatctgtgg	720
cttctcttct	taaaaatngaa	aaaaaaattg	tttaaaccca	naaggtctga	ataccaagc	780
ncctgaacn	anagaacaan	gccggagcac	cccctcccaa	atcccc		826

&lt;210&gt; 669

&lt;211&gt; 547

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(547)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 669

cattgtgttg	gggaaaaaat	gatttgtata	agcagtgggg	ctatttgcca	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aacctgaaat	tgacgctttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcatttag	ctctgatgag	tactacacc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagttag	taactcaaaa	cgagtgcac	tnggaagtat	cgacgctgtt	300
netggatnaa	attcccagct	tgctngcttg	ctnagccggg	gggcggtnaa	aaaaacatct	360
gcagcccnng	ggnaaaaacc	ttcgcatgtg	tcttacgtgt	ttacgttatt	ttatttcctt	420
nnagcaagc	nggganttg	ggactcgaaa	tgttacagtt	gggctgggga	tcgcccttgt	480
tacataaaag	ncgtccagaa	gagggacggt	tacaggcngg	ganctccaaa	ggtcagtccc	540

tgccatt

547

&lt;210&gt; 670

&lt;211&gt; 232

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(232)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 670

cgaactattt	agactaccta	ggaaaattat	tttagtatca	gaagaatata	aggggtgtag	60
tactcatcag	agctaaatga	gagcgcttta	aaaatggttag	tttgtcttcc	gccatttcta	120
cagaaagctg	caatttcagg	ttttcaacct	aataggtgat	atttaanaaa	aaaaaaaagc	180
aatcgcaaat	agccccactg	cttttacaaa	tcattttttc	cccaacacaa	tg	232

&lt;210&gt; 671

&lt;211&gt; 214

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(214)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 671

ctcccccttc	ntccttcgct	actnncatt	ttcnnaaatt	tntttcgcnt	atngggaaaa	60
acacccacat	tnttcancct	gcacagaaca	ngnnggggtg	tgtaaaatga	agggcttccn	120
cncctttctc	tattnaanaa	cactnaaana	gggangggct	aaaaccgcg	ngatntctac	180
nctatcgcg	gcgcttttgg	ngttggctag	aaga			214

&lt;210&gt; 672

&lt;211&gt; 328

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(328)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 672

ngancagcgg	ngtttaaact	ggcctctaga	ctcgaggaga	cncctgttgg	atggtggatc	60
acannctcgt	actactatac	aggacagagt	atcggganct	cttggnatgt	ggngcctgcc	120
aaccactgct	nctgttaact	gcgtatctga	agggactcgg	actggcttca	gaagaactac	180
cggctcgaat	gnaccatgga	tgattcncnc	tagttgaaaa	aaaactcagg	cacatgtatt	240
gccactgatg	actagcgcca	gactnctctc	ggctctntaa	cgagcccaca	tgncngtgtg	300
ncncccggtc	tgntccaga	agaggttc				328

&lt;210&gt; 673

&lt;211&gt; 223

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

240

<221> misc\_feature  
 <222> (1)...(223)  
 <223> n = A,T,C or G

<400> 673  
 gggggc aaag ctggctagcg tttaaactta agcttggtac cgagctcgga tcccnagac 60  
 attgtgcatg aaaatgcaaa ttgagtgtgg tctatantgc catentcacc tnctgncngc 120  
 tcaaaacaac ngctttctgc tgcaatgggt agggctcctn acncacggtc gcnnacggag 180  
 gccncttat cctentcggg nnggatccct ngaagcatnt tct 223

<210> 674  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(256)  
 <223> n = A,T,C or G

<400> 674  
 gnggggtcnt ngatgagcgc gcgtaatacn atcactntcn ggcgngntgg gtaccgggcc 60  
 cccctcnaa gcggccgccc ttttttntt ttttttcatn acatgataa ntcttnttc 120  
 taaacagacc acaccactan agttcctttn ctttngtacg gaattgagtt aaagtagagn 180  
 atacaatgca gggcttcnnc tctatttcac attccaggnt gggtcngnat ggatcgccc 240  
 tgctctccg atgggt 256

<210> 675  
 <211> 439  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(439)  
 <223> n = A,T,C or G

<400> 675  
 nnactagtcc agtgtggtgg aattccattg tgttgggctt gtatgggttt ttttgtctag 60  
 ttntttggga aatgttngtg ttactatntt ttggatatna tatatgatat gtatggccct 120  
 tctatgggct cctcanacng aactcaacca ttttccacaa aaccnattcc tcctttccct 180  
 tcatgactga gtgggtgttg tactatcng gaaactggga cattgtcctt cacatctntc 240  
 ccttanctgc ctngtccnat tgatgtcttt gagctntgan atgtctttgt taactntctc 300  
 ctntctctgt actgccggca naattaagca ccatntgtca caaaaagtat tgcgttacct 360  
 tcacgnatct gttingtncc atncttgctg cttctccngn ggaaaatagg ctnttctgga 420  
 aaccgaacng aanaaatac 439

<210> 676  
 <211> 587  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(587)  
 <223> n = A,T,C or G

<400> 676

241

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ngngngcctn  attaagcgcg  cgtaatacna  ctcactntgg  ggcgaattgg  gtaccgggnc      60
cccctcaagt  tnatntgccn  aacctctctt  ttggaataac  aaaagggtta  acacatatgt     120
cctcataggg  acgcgctttc  acacnttcct  gacngcttca  tanacntcat  tncatatttct    180
cctcagnaca  agttnaggcn  gaaggtgagg  canacnttat  aatttccatt  tcacaaatnc     240
ggaaagtgag  gctcaaaggg  nttaaaaaat  aacctgatac  aantcataga  gccggtntct     300
ggaanaagca  ggagcaaagt  ccaggcatcc  tgatccaagc  tnggtccact  gccttccact     360
ctggagaggc  ttcattctcc  acaaaggaag  ggacntgagt  ggctgganaa  tctcatggga     420
taaagacctc  agnatttcat  gctcctggaa  atcccatggg  ttgaacaaca  ggtntttggc     480
ccgtggttct  ntccctttgn  ccatctttta  accttggggt  aaatgatggc  ntctntnagc     540
nttttttttn  aaagagatng  aaattgaatg  attattngct  cattggg      587

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&lt;210&gt; 677

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(444)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 677

```

gtggggcatn  attaagcgcg  cgtaatacga  ctcactatag  gggcgaantg  ggtaccgggc      60
ccccctcgaa  gcggccgccc  tttttttttt  tttttactgt  ccaaactntc  tatngatnta     120
gttgaactgt  ncaacgattt  catgaaattc  tatacacana  gccttcaggt  ccagagagta     180
aaacaaattt  aaatttnttc  accanattgn  agcagncana  agcatccnat  natatccgac     240
tacaatgaat  natatgctna  nggtanctna  tttaccact  ntggggtctt  tanggtctgt     300
cacaaactat  tttcgtaaac  atcnntttta  anttnggtga  atggacctaa  tnccagataa     360
ntctatttna  tntacCctag  catncctgtg  gctnactttt  cgggctgtgt  tggcntactt     420
ttaggagaaa  attggtataa  atnn      444

```

&lt;210&gt; 678

&lt;211&gt; 670

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(670)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 678

```

actagtccag  tgtggtggaa  ttccattgtg  ttgggagcag  tttaaaaaaa  aaaaagacna      60
aatatacnac  tcttgatnaa  acataaaggt  acagtgtct  atgaggaana  gaaaagggtac     120
ctnaggatgc  aaaantacct  accacatggg  aaccgttngt  ccacactcat  tccnnanaaa     180
accgagtcct  ctcanttnca  cacgtgtacg  tttcagttgg  gaagtgtctg  ccattactcc     240
naagcctaga  accttcacgt  cctgaagggt  ctggaagggt  tttcagattg  cttaaganac     300
gcngcccttc  catattcntc  tccactaccc  nggggaacgg  aacaaatgga  gctgcgacng     360
ggaagcgtcc  cttcccntcc  gaacgctttc  tttcaaacct  gcctgccttc  cnggcgaatg     420
gaccggaagg  tttntctngt  tcctttcanc  ccnaattact  tcctgngttg  aaaattggcc     480
tgttggtttg  caaatgcngg  aatttgttta  ctttntcat  gtccgtgtgt  gnnacnaaccg     540
gctcnccttg  tgcctccctt  tngaaagggt  ttcacagggc  cccgcccttt  ctcttntaan     600
ngtcctaate  cggncnggac  cactcgggga  aaattttttc  ttttcgaaaa  gccgccccnt     660
ccgtccggtc      670

```

&lt;210&gt; 679

&lt;211&gt; 449

&lt;212&gt; DNA



242

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(449)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 679

actagtcag	tgtggtggaa	ttccattgtg	ttgggagtag	gtctactaca	ncctacttcc	60
cctatcatan	aaganccttan	caacnttcat	gatccccc	tcntannccet	tttcctcanc	120
tgcntcctag	tcctgtttgt	cctnttccta	acantcntaa	ganagatnac	taatnctact	180
atctctnacc	tcggaanct	acaanacgtc	tggaactatt	cngaccccat	gcancncat	240
ntcccatcgt	cctccagcc	cctncccttc	ctttacntta	ctnaacgaag	gtcgacgatc	300
cctcccntac	ctccnnncc	attgggnccc	aanggnactg	gacctcacga	ntacaccnac	360
tacggggnga	ctaagnctgn	aactccttac	atatntcccc	gttaccnccn	gaacncagcg	420
aacngcnaca	ccttggaant	caagaanta				449

&lt;210&gt; 680

&lt;211&gt; 670

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(670)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 680

tttcngtgtg	gtggaattcg	cggccgcgtc	gacgagaaga	nggaggagga	naaggagaag	60
gagaagaagg	agaanaagga	ggagaaggag	aagaaggaga	agaaatcatc	atcatcatca	120
tcactgtct	ngcaactatt	taagtttgc	antcccttga	aaacaggtag	ttttgtttca	180
atgtttggga	ccactnctga	cnatgannag	aanaccaata	aatgcttgat	naatgaaaaa	240
nccacttttt	acctgttaga	accctgaggc	taagagaant	gatgtgactc	gacttagtta	300
ccacaaacta	tgatcctagc	atnaattggg	gcattctcaac	acctcaactc	cctgtgcaag	360
aacagatttt	caatgtctac	tgatgatatt	aaatggatta	nttcctctct	ttacttctta	420
agggcagtaa	gntttatgaa	acaaaactat	ncagttccag	acgtttaacc	cacatagtgt	480
taatagtcac	cttcaacaca	cnactaaacc	cccaaaaaan	gntttttacg	gngtttcgac	540
agttttcttt	tctttttgac	ttgnttaaca	cccnnagaca	ctttgtntctn	tttcctntgaa	600
tcacancctt	cnaanancca	atggtncggt	tttttctcnt	tcngggccct	tccttnttn	660
aaaaccan						670

&lt;210&gt; 681

&lt;211&gt; 494

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(494)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 681

tcatggtgtc	cacagtctga	tgtgagcgca	ttaaatttaa	ggatctccgc	ccttctcctt	60
aaaactcagg	acttggaat	gancctagga	agcgccctc	ccctcccan	ccanaccaa	120
gccccggacc	gctgcgntc	cagctgcgcc	tagtgaaacc	gccgaattcg	aattcacact	180
cggngggccg	gcgaagggtg	gcgcgcgccg	gggagcgccg	gggcnagccc	gagggactgc	240
aagccaanaa	nggaggcatg	ggtggcgggg	ggcgccgtct	gatccaggaa	ggagcggagg	300
cgccgatcac	acactcttna	gacgcctgc	ccgcgcctgg	ccagcgcgca	gnetgcagga	360

243

```

cgcgcgaggc aggaactcgc tggagtttgc caagccccc gnetctggaa agtntgtagc 420
tccctttcgg ancgnctctt ctggcccttt gggacgggtg tgcattggg cgggggtctg 480
tataaggggg ggac 494

```

```

<210> 682
<211> 263
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(263)
<223> n = A,T,C or G

```

```

<400> 682
tgatcattca agcgnatgnc gnataacgat tgctnagccc aacctttcat agggtcgttc 60
ctttgggaat nggatgtcta ttgaatggca gggatagggg cactcggcat tcgcctctgg 120
tacagttttg catatatatc ctcacgcgca gcgagcgtag gggancgtta agtttgggga 180
aatgccnccg catgnccctn cggagctta aacccccaac aatnccatt ttnaaaaaag 240
ntttnttant taaaaaaaaa aac 263

```

```

<210> 683
<211> 255
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(255)
<223> n = A,T,C or G

```

```

<400> 683
cttgccccgc atgcacagac ntntttacgg acacnctact ccaagngagc ctgnanctgt 60
ctacgggtcaa nctctaagg tngncantgc cacanatggc atagtcccg gggcggtnan 120
tctggantgc tctctgcact tgaacntaaa gcgcntttca aganaggnc aatngcctgc 180
ctcttgacaa cnaacaancc cacaccnacc tangaccctn tangcaagga ctggattctg 240
naaatgcaat acaca 255

```

```

<210> 684
<211> 922
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(922)
<223> n = A,T,C or G

```

```

<400> 684
acctttcatt tcatgtgctt ctattttctt acatctttta catgactaag ggattaatga 60
aatcacctct tcataatcat gaccataatt tcatccaaca agtactcaag tttggtgtta 120
gcactttatt aatgcttacg aattctctct ctctccctct ttctcttttc cttagtcctt 180
gcacaataag gatttttgaa tgtataatat catcttaggt aagctttcat atggttttgg 240
catatgaagc ttatgactgt cataagccat accaagcctg tggagtatgg catgattttc 300
attacataat ccaatgaaaa tagacttatt ttaaatccct aactttgtag ttttaatttg 360
tatttcaact tcttgaaatt aacagctagt acttatccat caacagcagtc tcctactgac 420
atgaagcaag ttgttgaatg cagtaganca tgaatgaaag catttaatgt tanacaaaaa 480
tggggtgatac ccaagcattc tgaattattt gcatcaagga atgggacatg tacattagt 540

```

244

```

gcatcatttc taccaatatg tgacttgaat tgttttttta aaaaaaggan aatgantttc 600
tcaatttgct ttaaaaaatt ttnaaaaagt tcaatggcat gctgctttgt ctggacttaa 660
tttattaaca attnttaanc cttccttaag gacanaattt tgggtgttcag gatcnccctg 720
aagggtctta tttttnatan nattccaaac ccaaaagggtg gtttaaaatg gnggggttcc 780
ccccncnaaa atttggaccg gcttttttat atttaaaaaa nttncnnttt gngtttgaaa 840
nctnaatacc aattaagggg gaattttacc tnccagtggg aaaaaaaaac nctngcctt 900
naaaaaattc ccnggagnca at 922

```

&lt;210&gt; 685

&lt;211&gt; 531

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(531)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 685

```

tgaggctctg taaaactgtt cctctgctag gcatacttca tattctctat attaaactca 60
tctttaattg gcatggaaga ttcattgttc caaatctcag atgaagatcc tatattggat 120
gcaattaagc ctggcagcgc cctcaaaaga cagtcttgtc actgctagcc acagccagga 180
cacagtaaca gttccttcta gtgaccnag accataanaa atananatct aaagaattct 240
gactccaaag gcattagccc attcctggta ttgccaatTA tgatagaaaa aattgccaaag 300
ctcctgggac atggaaatac actcagtaca tttgagaact ggagaactan tttccaaaat 360
agtatgaaga catganggtg attgtagata tntgagtttg gagaanttga gggaaatcng 420
attacacatg tttactacaa gagatgttna taagttaaaga aggcctgata tacaatctaa 480
cagacnantg agataaatct taantcacia ctgacntccc ttttggggcg g 531

```

&lt;210&gt; 686

&lt;211&gt; 336

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(336)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 686

```

gngncctna tgagcgcgcg taatacgatc atatagggcg aattgggtac cgggcccccc 60
tcaagaacac tacaagctat gtctcttct canagagccc tgaantttta acatattgaa 120
agctctnatc ttgccaaana actccactta acttcaaaac acaccctcca cacacatcat 180
gatcaactna gatcttactg aaccagaatc ctnaatggca tacttcagga acaggggtcc 240
anagaagcag ttctcaaant gcagctnaaa aagaaactga aaaccaatt catgcaanac 300
ctagggctta tttgagagca ttttccagtg cagatt 336

```

&lt;210&gt; 687

&lt;211&gt; 271

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(271)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 687

245

```

aatctgcact ggaaaatgct ctaaaaataag ccctaggtct tgcatagaatt gggttttcag      60
tttcttttta agctgcactt tgagaactgc ttctctggac ccctgttcct gaagtatgcc      120
athtagatt ctgggttcagt aagatctcag ttaatcatga tgtgtgtgga ggggtgtgtt      180
tgaagtttag tggagttctt tggcaagatc agagctttca atatgttnaa acttcagggc      240
tctctgagaa gaggacatag cttgtagtgt t                                271

```

<210> 688  
 <211> 740  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(740)  
 <223> n = A,T,C or G

```

<400> 688
tgatgaagcg cgcgtnttac nactcactat nggggcgaan tatgggtacc gggnccccct      60
cgaagcggcc gccctttttt tntttttttg tgagagttta aataaaatat ttgagtttaa      120
tttaaagttt gagtttaatt aaaatatatg gcatatccca agttgggctt tgcanaaaga      180
acacttttca ggaactgtta gttggtgtac caggaactca gaagggtcct gttattaaat      240
atatttgtaa aatgcatgga ttctctgaan atcncctctgc atgtgagcaa cacttacatc      300
ncaaaccaaa attggcattg catacatnaa ccaatatttc ccaaacattt ctgggttatgg      360
cccacccctt ttgtgtanta cttattgctg ttttttgtaa ccctggggaa attacttaaa      420
atattcagct ggaaattaca ggcgttactt ttaaggganc agaattaca gtgactccca      480
aaattgcaag tgttgattac tatttaagaa ccaagaatt tgaaagaaat tttgaaaagt      540
gaaaacngga aatnttaaatt gacttctcaa attttgaaa ctcnngnaaa catctccact      600
ttggtnccct tccttttaaaa attggctaaa aattntttnt tatncccacc ccattggaan      660
tncccccccc ctggaacaat tggattcccc tatttcctaa aaaacggccn ccccccccg      720
gnggaacncc nacttttgn                                740

```

<210> 689  
 <211> 635  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(635)  
 <223> n = A,T,C or G

```

<400> 689
actagtccag tgtgggtgaa ttccattgtg ttgggattac atatactttt agcaattttt      60
aaagaagtgt acaaagttga gatgtttcct gagctctcat atatctgana atgtcatttt      120
acatctccgt cttcacctct caaaacttct ttcaattctt tggctcttaa tagtaatcaa      180
cacttgcaact ctggagtcac tgtaattctt gtccttttac agctacnctt gttatttcca      240
gctgaatatt tttagttatt tcccagggtt ccaaaaaaca gcaataagta ctacacaaag      300
gggggtggcc ataaccagaa atgtttggga aatactggct catgtatgca atgccaaatc      360
tggtttgcna ttgtantgtt gctcacatgc agagtgaatc ttcaaanaat ccatgcattt      420
tccaaatata ttttaataaca gggaaaccttc tganttcctg gntacaccaa ctaacagttc      480
ctgaaaaatg ttctttctgc aaaacccaac ttgggggatat gccatatatt ttaattaaac      540
tcaaacttta aattaaactn caattatttt attttaaact cctcaaaaaa aaaaaaaaaa      600
agggggggcc cttccaangg ggggnccggt tcccc                                635

```

<210> 690  
 <211> 3923  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 690

acagaagaaa	tagcaagtgc	cgagaagctg	gcatcagaaa	aacagagggg	agatttgtgt	60
ggctgcagcc	gagggagacc	aggaagatct	gcatggtggg	aaggacctga	tgatacagag	120
gaattacaac	acataacttt	agtgtttcaa	tgaacaccaa	gataaataag	tgaagagcta	180
gtccgctgtg	agtctcctca	gtgacacagg	gctggatcac	catcgacggc	actttctgag	240
tactcagtgc	agcaaagaaa	gactacagac	atctcaatgg	caggggtgag	aaataagaaa	300
ggctgctgac	tttaccatct	gaggccacac	atctgctgaa	atggagataa	ttaacatcac	360
tagaaacagc	aagatgacaa	tataatgtct	aagtagtgac	atgtttttgc	acattttccag	420
cccttttaaa	tatccacaca	cacaggaagc	acaaaaggaa	gcacagagat	ccctgggaga	480
aatgccccgc	cgccatcttg	ggatcatcgat	gagcctcgcc	ctgtgcctgg	tcccgttgt	540
gaggggaagga	cattagaaaa	tgaattgatg	tgttccttaa	aggatgggca	ggaaaacaga	600
tcctgttgtg	gatatttatt	tgaacgggat	tacagatttg	aaatgaagtc	acaaagttag	660
cattaccaat	gagaggaaaa	cagacgagaa	aatcttgatg	gcttcacaag	acatgcaaca	720
aacaaaatgg	aatactgtga	tgacatgagg	cagccaagct	ggggaggaga	taaccacggg	780
gcagagggtc	aggattctgg	ccctgctgcc	taaactgtgc	gttcataaacc	aaatcatttc	840
atattttctaa	ccctcaaaac	aaagctgttg	taatatctga	tctctacggg	tccttctggg	900
cccaacattc	tccatataatc	cagccacact	cattttttaat	atttagttcc	cagatctgta	960
ctgtgacctt	tctacactgt	agaataacat	tactcatttt	gttcaaagac	ccttcgtgtt	1020
gctgcctaata	atgtagctga	ctgtttttcc	taaggagtgt	tctggcccag	gggatctgtg	1080
aacaggctgg	gaagcatctc	aagatctttc	cagggttata	cttactagca	cacagcatga	1140
tcattacgga	gtgaattatc	taatcaacat	catcctcagt	gtctttgccc	atactgaaat	1200
tcatttccca	cttttgtgcc	catttctcaag	acctcaaaat	gtcattccat	taatatcaca	1260
ggattaactt	tttttttttaa	cctggaagaa	ttcaatgtta	catgcagcta	tgggaattta	1320
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gatttttttt	ccagtataaa	gttaaaatgc	ttagccttgt	actgaggctg	tatacagcac	1440
agcctctccc	catccctcca	gccttatctg	tcatcaccat	caaccctccc	cataccacct	1500
aaacaaaatc	taacttghtaa	ttccttgaac	atgtcaggac	atacattatt	ccttctgcct	1560
gagaagctct	tccttgtctc	ttaaatctag	aatgatgtaa	agttttgaat	aagttgacta	1620
tcttacttca	tgcaagaag	ggacacatat	gagattcatc	atcacatgag	acagcaata	1680
ctaaaagtgt	aatttgatta	taagagttta	gataaatata	tgaatgcaa	gagccacaga	1740
gggaatgttt	atggggcacg	tttgtaagcc	tgggatgtga	agcaaaggca	gggaacctca	1800
tagtatctta	tataatatac	ttcattttctc	tatctctatc	acaatatcca	acaagctttt	1860
cacagaattc	atgcagtga	aatccccaaa	ggtaaccttt	atccatttca	tggtagtgac	1920
gcttttagaat	tttgggcaaat	catactgggc	acttatctca	actttgagat	gtgtttgtcc	1980
ttgtagttaa	ttgaaagaaa	tagggcactc	ttgtgagcca	ctttagggtt	cactcctggc	2040
aataaagaat	ttacaaaagag	ctactcagga	ccagttgtta	agagctctgt	gtgtgtgtgt	2100
gtgtgtgtgt	gagtgtacat	gccaaaagtgt	gcctctctct	cttgacccat	tatttcagac	2160
ttaaaacaag	catgttttca	aatggcacta	tgagctgcca	atgatgtatc	accaccatat	2220
ctcattatct	tccagtaaat	gtgataataa	tgatcatctgt	taacataaaa	aaagtttgac	2280
ttcacaaaag	cagctggaaa	tggacaacca	caatatgcat	aaatctaact	cctaccatca	2340
gctacacact	gcttgacata	tattgttaga	agcacctcgc	atttgtgggt	tctcttaagc	2400
aaaatacttg	cattaggtct	cagctggggc	tgtgcatcag	gcggtttgag	aaatattcaa	2460
ttctcagcag	aagccagaat	ttgaattccc	tcacttttta	ggaatcattt	accaggtttg	2520
gagaggattc	agacagctca	ggtgctttca	ctaattgtctc	tgaacttctg	tccctctttg	2580
tgttcatgga	tagtccaata	aataatgtta	tctttgaaact	gatgctcata	ggagagaata	2640
taagaactct	gagtgaatc	aacattaggg	attcaaagaa	atattagatt	taagctcaca	2700
ctgggtcaaaa	ggaaccaaga	tacaaaagaac	tctgagctgt	catcgtcccc	atctctgtga	2760
gccacaacca	acagcaggac	ccaacgcagt	tctgagatcc	ttaaatcaag	gaaaccagtg	2820
tcatgagttg	aattctccta	ttatggatgc	tagcttcttg	ccatctcttg	ctctcctctt	2880
gacacataatt	agcttctagc	ctttgcttcc	acgactttta	tcttttctcc	aacacatcgc	2940
ttaccaatcc	tctctctgct	ctgttgcttt	ggacttcccc	acaagaattt	caacgactct	3000
caagtctttt	cttccatccc	caccactaac	ctgaaatgct	agacccttat	ttttattaat	3060
ttccaataga	tgtgcctat	gggctatatt	gctttagatg	aacattagat	atttaaagct	3120
caagaggttc	aaaatccaac	tcattatctt	ctctttcttt	cacctccctg	ctcctctccc	3180
tatattactg	attgcactga	acagcatggt	ccccaatgta	gccatgcaaa	tgagaaaccc	3240
agtggtcctt	tgtggtacat	gcatgcaaga	ctgctgaagc	cagaaggatg	actgattacg	3300
cctcatgggt	ggaggggacc	actcctgggc	cttctgtgatt	gtcaggagca	agacctgaga	3360

247

tgctccctgc	cttcagtgtc	ctctgcattc	cccctttcta	atgaagatcc	atagaatttg	3420
ctacatttga	gaattccaat	taggaactca	catgttttat	ctgccctatc	aattttttta	3480
acttgctgaa	aattaagttt	tttcaaaatc	tgctccttga	aattactttt	tcttacagtg	3540
tcttggcata	ctatatcaac	tttgattcct	tggtacaact	tttcttactc	ttttatcacc	3600
aaagtggctt	ttattctctt	tattattatt	attttctttt	actactatat	tacgttggtta	3660
ttattttgtt	ctctatagta	tcaattttatt	tgatttagtt	tcaattttatt	tttattgctg	3720
acttttaaaa	taagtgattc	ggggggtggg	agaacagggg	agggagagca	ttaggacaaa	3780
tacctaatgc	atgtgggact	taaaacctag	atgatgggtt	gataggtgca	gcaaaccact	3840
atggcacacg	tatacctgtg	taacaaacct	acacattctg	cacatgtatc	ccagaacgta	3900
aagtaaaatt	taaaaaaaag	tga				3923

<210> 691  
 <211> 882  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(882)  
 <223> n = A,T,C or G

<400> 691						
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 <211> 235  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(235)  
 <223> n = A,T,C or G

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 <213> Homo sapien

248

<220>  
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 <223> n = A,T,C or G

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<210> 694  
 <211> 204  
 <212> DNA  
 <213> Homo sapien

<400> 694  
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<210> 696  
 <211> 317  
 <212> DNA  
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<220>  
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<223> n = A,T,C or G

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<210> 697

<211> 246

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(246)

<223> n = A,T,C or G

<400> 697

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ctttct						246

<210> 698

<211> 3674

<212> DNA

<213> Homo sapien

<400> 698

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&lt;210&gt; 699

&lt;211&gt; 2051

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2051)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 699

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&lt;210&gt; 700

&lt;211&gt; 2841

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2841)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 700

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&lt;210&gt; 701

&lt;211&gt; 3228

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

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&lt;222&gt; (1)...(3228)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 701

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&lt;213&gt; Homo sapiens

&lt;400&gt; 702

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 703

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&lt;213&gt; Homo sapiens

&lt;400&gt; 704

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&lt;211&gt; 6976

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 705

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&lt;210&gt; 706

&lt;211&gt; 123

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 706

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Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val
      20              25              30
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
      35              40              45
Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu Thr Gly
      50              55              60
Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala Ser Leu
      65              70              75              80
Tyr His Arg Glu Lys Gln Val Leu Ile Gly Gln Trp Val Glu Ser Gly
      85              90              95
Trp Glu Gly Trp Ser Gly Phe Leu Gly Gly Gln Leu Ala Gln Asn Leu
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260

Val Ser Gly Lys Gln Leu Trp Arg Met Leu Leu  
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&lt;210&gt; 707

&lt;211&gt; 150

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 707

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 Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val  
 35 40 45  
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Glu Ser Leu His Pro Pro  
 50 55 60  
 Ser Phe Leu Phe Gln Ile His Ala Thr Trp His Val Gly Gln Glu Tyr  
 65 70 75 80  
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 85 90 95  
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 100 105 110  
 Lys Lys Arg Ile Pro Arg Thr Tyr Pro Ser His Leu Trp Ile Pro Gly  
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&lt;210&gt; 708

&lt;211&gt; 371

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 708

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 35 40 45  
 Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp  
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 Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val  
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 Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro  
 115 120 125  
 Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu  
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 Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser  
 145 150 155 160  
 Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu  
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261

Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala  
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 Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala  
 195 200 205  
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 210 215 220  
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 225 230 235 240  
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 290 295 300  
 Gly Ser Arg Pro Pro Glu Thr Thr Leu Gly Ala Val Ser Gly Leu Val  
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262

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263

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 <223> n=A,T,C or G

<400> 715  
 tactctanag gatctncgng tcatntggat tctatntcga ctcactctag ggctcnagcn 60  
 gtcngccggg caagttattc ggatcgctcg gntccgagct tcgcaattaa ntgtgccatc 120  
 gttctncaac gttcctgact nggaancccc ngcngttcng atccncnggt acctagctcc 180  
 anntcccccg tntccttctt ggngtntcat naangaggac cncctctgat cnccttctct 240  
 taatctgcnc acnctgaacg nccaatggac atngtgcgtt taatntanna ggcccgnntc 300  
 gngtgccctt cccgtnannt cagctc 326

<210> 716  
 <211> 122  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(122)  
 <223> n=A,T,C or G

<400> 716  
 nntgcgtcgc ctgngcgtnt actctagatg atctgantag tcatatggat totaatacga 60  
 ctcannatag ggctctagcg nggatncnga ttcgtcttcc ngattcantg acnccggtan 120  
 ca 122

<210> 717  
 <211> 203  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(203)  
 <223> n=A,T,C or G

<400> 717  
 cntgcatgcc tgcaggctcga ctctagagga tctactagtc atatggatcg agcggccgcc 60  
 cgggcagggtg tnaatgataa anatgcatca tactanccta cagaanggag agataatgtt 120  
 ngntggacca ngttggtttt cttgcgtgtg tgtggcagta gtaagttatt agtttttana 180  
 atcantaccg ccctccgcac cac 203

<210> 718  
 <211> 168  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature

264

&lt;222&gt; (1)...(168)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 718

```

ggcagganga tcncttgagc ccnngaggtc gaggtacag tgagccanga gtgcactact 60
gtnnccgcct ccgcatncac gngtggtccg atccccgggt accganctng anttcactgg 120
antttttttt aancgtnttg antggtacna cctcgcantc cctggctg 168

```

&lt;210&gt; 719

&lt;211&gt; 210

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(210)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 719

```

cancgtcgnc ataacacgta ttttntgatn aagattctna ctgacccatn aantctacnt 60
ctcaagctct tncanngtcc agtnaangga atgtgtatnn gtngggatnc cacanaaaaa 120
aganatntcg gncgcttcat tantcatcct tottaccan ntctctngat nncagntng 180
ancntgaacg cacactacng gatntctcca 210

```

&lt;210&gt; 720

&lt;211&gt; 131

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(131)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 720

```

tccatcctaa tacgactcac tatagggtcg ccaacctgcc atccactact gaggaagacc 60
cgnaactta ggggctcact gcgagccacc ggcacaggt cgtatagggc aaagcacng 120
gaagcacccc t 131

```

&lt;210&gt; 721

&lt;211&gt; 121

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(121)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 721

```

tccatcctaa tacgactcac tatagggtcg ntgantnctg gcgaaaggct tacaattaag 60
naggaaaaan ganccaacaa ctaaaaaaaa nncggncgtg hcagcttnga tgactngtcc 120
a 121

```

&lt;210&gt; 722

&lt;211&gt; 246

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

265

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(246)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 722

```
anctggagtc ggcgctgca gtcacattgt ggatccanaa aatcggcaca agctctcntg 60
gnttcntcga tatgaanaac actaatccca tgtngtntgn gtctccgtga ttcattccctc 120
gcacnggtcc ccntocnaac cnttgcatag gtgttatgtt gtantctccc cagtgcacaa 180
agattnacac tctctcantg tctganatat gcacgagttc attgtcctgt cnccgtnaac 240
atcaag                                     246
```

&lt;210&gt; 723

&lt;211&gt; 160

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(160)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 723

```
cctccggaaa atccaantag agtaantncn ctctaattccg gggnaattgg nggggttnnat 60
acgtcctcct cccccagnt aggattnana aaaggntccc cagancaaaa nctccaaagt 120
gnatcnanta gccgtncccg anatincaacg cccctacgtc 160
```

&lt;210&gt; 724

&lt;211&gt; 156

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(156)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 724

```
tnanccnata tacaccaaatt tctgattcta aantcccacc caagggaaaa aagttgagaa 60
gagcctttcc actttttctac taataaaaaa atgcaccagc ccctaccann agtgnggaaa 120
acctccttag gcccttgnnt ggaacaancg aaaatc 156
```

&lt;210&gt; 725

&lt;211&gt; 347

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(347)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 725

```
aganggttnt atncatgctg tactcgcgcg cctgcagtcg acactagtgg atccaaagaa 60
ttcggcacga gagacggtgc gcatgggacc gagggcccca gccgngagg cgccgcccgc 120
gagcccgcg ncagagcgcc catcagtagc gtccgcaccg ggnagcccg gntctcgccc 180
gagccgtggg cgcgcccag gggcgggctc gcctcccgc gtccctcgca gctctgcgg 240
```



266

gcccgagccc gcgccgtcgc cgccgccgnc ttgccgctcg gncgcgcggg nccggnaaac 300  
gcggtcgagg tctggatgng gcanngcccg cncctntcgc tgagcct 347

<210> 726  
<211> 162  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(162)  
<223> n=A,T,C or G

<400> 726  
ttgggtgggt tgggtggggg naaatttncc catttgggtg ggtttggggg ggnaaatact 60  
tccgccttt tngtnccca aaganacnaa gggggagtcc cttnatagag gnagngcgat 120  
nctncaaac nacntngact ttgnccatgg ggagnaaggt gg 162

<210> 727  
<211> 120  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(120)  
<223> n=A,T,C or G

<400> 727  
gtgtgggtgg ggaattccat tgtggttggg ggnaaatctc cgcttgtcca aagnacaggg 60  
ggggtcnctt anagngnagg gggttcctcc ccaccacttg ncttgnccat tngagnaag 120

<210> 728  
<211> 130  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(130)  
<223> n=A,T,C or G

<400> 728  
gaccactgc agcgttnaac ttagcttggg ccgagctcgg atccctagtc cgtgtggtgg 60  
aattccatgt gtcgagagag gggcaaatac nctccaanac ancnccctca tgctcnacac 120  
atattcgcat 130

<210> 729  
<211> 182  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(182)  
<223> n=A,T,C or G

<400> 729

267

```

cngactgctn gcgtttaaac ttaagcnagg taccgaacgg ggatnnacga ctantgatcg 60
gctggctgct tccagtcgat tanatttgtg aaaaagctga accncngccn gttaaggggg 120
annatgcaaa anatncatcc nctgccccn taaactgntc tntccnaggg aaaaaangga 180
ag 182

```

```

<210> 730
<211> 678
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n=A,T,C or G

```

```

<400> 730
cactcncact ccggacctag gcnccttcacc actgctctct tctcctcct cctcctcnc 60
ctcggggctg ggggaccttc cccagtgacc atctcacttt ggctgaancc cactcggggc 120
agcctgagtt tggggctctt ggccttctca cctcctcctg cccctcctt ggcccgacc 180
aggccaaacc ggggcagccg taccttgagc ttgtgtccgg cctctccctc cccctctgcc 240
acctggtact cggcatggtt gccccggga tggcgagagc tccacgtcgg gcagtggaa 300
gcagaaagta cgctcgccc ctgggggctg ctctcagca cctcgcgcc ccacctagc 360
tctggcccc agtgtgggca acttcagcct cagccaccc tcgctgtgg ccgctcgcc 420
cgctgtgccc tctcggtta gcccacgtc caactcaagc tggggcactg tcacggtgg 480
catcttaag acacctcac ccaccagcag ctcaccacct gcaacctggg ctccaggcaa 540
aaaaagggtc acctggggca nctgaacct gtacctgtg tgccctctgc tgaangaat 600
gttatctgaa cctgctgccc tgggggtact gccttccaa aaccgggtca antccacctg 660
ttggaaggna aatncccc 678

```

```

<210> 731
<211> 135
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(135)
<223> n=A,T,C or G

```

```

<400> 731
gagatccgac gtcacccct tccggcggcc caagacgctg caactccga ggngcccaa 60
atatctttgg aagagcgctc ccagcccaac acaatggaat tccaccacac tggntagt 120
gatccgagct aagcc 135

```

```

<210> 732
<211> 660
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(660)
<223> n=A,T,C or G

```

```

<400> 732
gcttgggtacc gagctnggat ccctagtaac ggccgccagt gtgctggaat tcggctttct 60
tcaatcagnt nacgagctgc atggtctgct aacattgtca taattgctgg catagattac 120
tgaaaataaa gaaaaaaaat tgaagctgcc tatcaagttt tggattatc aaaaacttc 180

```

```

tacaagttat tttacttcaa ccatgttatt acaaatattt taatgaatac tttagagact 240
ttaattacaa aaaactgaga tagtaaaagc aagtaataaa agctgaaatt acttagctat 300
ttgataatta cataaattat tatggtccat tcaacttttc tagtgtttag tttatacacc 360
aggaagactt tcctattcta ctaacattta taaagtatgc taacctatta tttaaacgca 420
tcctactatta ggattttatg gcctaaaacg tgatacagtt cagtatcttg atgtcaaaac 480
tttttaagca agtagggatt aagttcaagt gaatgtgatt ttctttcttc ccagtagggg 540
cttctgaata actcagnaaa gctcacttcc attatcttac tttataaaaa aatgctataa 600
gacagaatgg gccgacgtgg nggctccacc tgtatccacc tttggaggcg agnggcgaat 660

```

```

<210> 733
<211> 836
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(836)
<223> n=A,T,C or G

```

```

<400> 733
aattaatgac tttttttccg ccctgccaag ctagtttgtc taaatataat gtaaagaaat 60
tagctactca ttttctggtc cacgaagggt cctaaatgg gaagaagtgg agatctgacc 120
ttgttagttc taaatacact aaactgggag tgccatggat ggctttcagg atgtcctgaa 180
tcctctataa ttgtatacaa aatcgtgagt ttttaaaaac tgggttagag ctattgggtc 240
ctcagagtct caggcatctt agaccccaa aaagggttaag gactactgac ttaaccaatt 300
aggtttgagt ggcattggct ttgaagaaaa gcagaggaaa gatataatatt ataattctgg 360
gcaacaaaaa agtggatgtg tgccagcatc ttagagtaga atcctcttaa aaggatagca 420
ctgcatatga actagtaggt ttaaccaggt gcatatttag gcgaagtagc tcatttttct 480
gttagaattc ttttttattt gggaatgggc aagcttttac agcttttacc ttgccaatga 540
atacctggaa tttaaaaaat cttgttaggc atattgcca taaagttttt tttcctagat 600
catatatcca gtaaatatgt ttgtagcttt atttcaatcc cccaattcat tgagggttga 660
aacaatttga atggtttgag tgtagaagct aagttatttc tgtagaggct aagggcattt 720
ataccaanat atgttagact tgnngntcct gttaaccatg ctgtanacaa taggaattac 780
tgtatatcca cattttaatt ttaacatctt ctgctttgnt gntggtttga gangga 836

```

```

<210> 734
<211> 694
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(694)
<223> n=A,T,C or G

```

```

<400> 734
nagtnctatt tncactaaac tngnagtgcc ttggatggct ttcaggatgt cctgaatcct 60
ctataattgt atacaaaatc gtgagttttt aaaaactggg ttagagctat tggttcctca 120
gagtctcagg catcttagac ccccaaaaag gttaaggact actgacttaa ccaattaggt 180
ttgagtggca ttggctttga agaaaagcag aggaaagata tattttataa ttctgggcaa 240
caaaaaagtg gatgtgtgcc agcatcttag agtagaatcc tcttaaaagg atagcactgc 300
atatgaacta gtaggtttta accagtgcac atttaggcga agtagctcat ttttctgtta 360
gaattctttt ttatttggga atgggcaagc ttttacagct tttacctgc caatgaatac 420
ctggaattta aaaaatcttg ttaggcataat tgcccataaa gtttttttct ctagatcata 480
tattcagtaa atatgtttgt agctttattt caatcccca attcattgag ggttgaaaca 540
atttgaatgg tttgagtgtg gaagctaagt tatttctgtg gaggctaagg gcatttatac 600
caagatatgt tagactttgt gttcctgtta accattgtcg tagacaatag gaattactgt 660
atatccacat ttttaatttt aacatcattc tgctc 694

```

269

<210> 735  
<211> 126  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(126)  
<223> n=A,T,C or G

<400> 735  
ncnttgaaac nggttgacca gacttcaggc ctgtgcgctc aatcgtggag aatctcgtgc 60  
cgaattcggc acgagtctct ctctctctct ctctctctct ctctctctct ntctctctct 120  
ctctct 126

<210> 736  
<211> 165  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(165)  
<223> n=A,T,C or G

<400> 736  
cagaagcctt taaaccggtt ngaccagact tcaggcctgt gcgctcaatc gtggagaatc 60  
tcgtgccgaa ttccgcacga gtctctctct ctctctctct ctctctctct ctctctctct 120  
ctctctctct ctctctctct ctctctctct ctctctctct ctctc 165

<210> 737  
<211> 125  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(125)  
<223> n=A,T,C or G

<400> 737  
ggnagcccct ttaaccgttt gtccagactt caggcctgtg cgctcaatcg tggagaatct 60  
cgtgccgaat tcggcacgag tctctctctc tctctctctc tctctctctc tctctntctc 120  
tctct 125

<210> 738  
<211> 137  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(137)  
<223> n=A,T,C or G

<400> 738

270

```

ggagnncnctt gancaggatg accgacttca ggccctgtgcg ctcaatcgtg gagaatctcg 60
tgccgaattc ggcacgagtc tctctctctc tctctctctc tctctctctc tctctctctc 120
tctctctctc tctctctc                                     137

```

```

<210> 739
<211> 970
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(970)
<223> n=A,T,C or G

```

```

<400> 739
aggcctatatt aggtgacact atagaacaag tttgtacaaa aaagcaggct ggtaccggtc 60
cggaattcgc ggccgcgtcg acggcccttn gtgccactag ntctttcatt cttccccccc 120
atcaatcagt gaacttttta gcctactcaa agctttgctc caatgcatag gatttatgat 180
tgtggggatt tccagataat ataaatattc aacatgaata ttttaaatta aggcatagaga 240
catttttctt aactgagcat agccatgaac ctctcacgtc tgttcctctg tgtcagtttg 300
tancactgaa tacagcagcc ctctctaaaag tccaggcagt gcacagggtc tgacatgatg 360
aagtgcgctg ttgctatggt gattttgcag ctggccaaat agtcactggg tgattttacc 420
cagcaggaga tttttgcaaa aatttcctgg gtgagagtga aatcaaactc ctattttgnt 480
tctcctctgc aagctgnagt taagatggat taatgagtac ttttagatta attaactctg 540
aagagaaaat gggagaaaag tgaggaaggt tgttggcaga agtcattgct ggaatccttc 600
tgaaggaggt actgacttca cttgcaaaga cnagagacta naagacaatg aagttaaact 660
tggcctgtct ctcatatgat agatgctgag agtcaggntc agggaaattt aattctgtca 720
tacgcataatn ggattatgtg gtcattggatt tgttggcact aaccngcctn taatcagnat 780
aagaaaagtg ttttggtaga naaagaaaat tatggcccag aaaaacctgg aanacttgga 840
aaaaatgntn gggggccttg ggtggtggtc tnaaaanacc ccctggggat nttaaacc 900
aaantgaaga agggaaaaat ntttcccnct nttttntttt tttgccccct tgggattggg 960
ttttntttcc                                             970

```

```

<210> 740
<211> 739
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(739)
<223> n=A,T,C or G

```

```

<400> 740
gntgtcnaaa aagcaggctg gtaccgggtc ggaattcgcg gccgcgtcga cggcccttgg 60
tgccactagt tctttcattc ttcccnccca tcaatcagtg aacttttttag cctactcaaa 120
gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180
acatgaatat tttaaattaa ggcatagagc atttttccta actgagcata gccatgaacc 240
tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
ccaggcagtg cacagggtctt gacatgatga agtgacgtgt tgctatgggtg attttgagc 360
tggccaaata gtcaactggtt gattttaccg agcaggagat ttttgcaaaa atttcctggg 420
tgagagtga atcaaaactcc tattttgttt ctctctgca agctgnagtt aanatggatt 480
aatgagtact tttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540
gttggcagaa gtcattgctg gaatccttct gaaggagta ctgacttcac ttgcaaagac 600
aagagactan aagacaatga agttaactt ggccctgtctn tcatatgata gatgcttgag 660
agtacaggnt cagggaattt ttaattctgn catacgcata ttggattatg tgggtcatgg 720
ctttgtttgg cncctaacc                                     739

```

271

<210> 741  
 <211> 1171  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(1171)  
 <223> n=A,T,C or G

<400> 741:  
 gccttgnggt gacactatag aacatgtttg tacaaaaaag caggctggta ccggtccgga 60  
 attcgcgcc gcgtcgacgg cccttnntgc cactagtctt ttcattcttc cccccatca 120  
 atcagtgaac tttttagcct actcaaagct ttgctccaat gcataggatt tatgattgtg 180  
 gggattttcca gataatataa atattcaaca tgaatatttt aaattaaggc atgagacatt 240  
 tttcctaact gagcatagcc atgaacctct cacgtctgtt cctctgtgtc agtttgtagc 300  
 actgaatata gcagccctcc taaaagtcca ggcagtgac aggtcttgac atgatgaagt 360  
 gacgtgttgc tatggtgatt ttgcagctgg ccaaatagtc actggttgat tttaccacgc 420  
 aggagatttt tgcaaaaatt tcctgggtga gagtgaatc aaactcctat ttgtttctc 480  
 ctctgcaagc tgtagttaag aagggtataa tggagtactt ttaagaatt aaattaacct 540  
 cttgaaagaa gaaaaaatgg gggaagaaaa aaagtgaag ggaaaagggn ttggttttgg 600  
 gccnaaaaaa aagttccaan tttnngcctt ggggaaaaat tccccntttt ccttggnaaa 660  
 aggggggnaa ggttaancct tgggaacctt tttccnncct tttnngccca aaaggggaac 720  
 ccanggggaa agaaccttta gnaaaggaa acccatttgg gaanggggtt naaaacctt 780  
 ngggcccccg ggcctcctc caanaaggga aaaaaaaagg cctggaaaan gtaccagggt 840  
 ttcangggna aaanttaaaa ttcttgcca atancnccat aattgggaat tatggggggg 900  
 ccattgggctt ttggtttggg cncctaacc cgcnttttaa attcaaanna aaaaaaagng 960  
 gtttggaaaa nnaaaanaaaa aaaattnaan ggnccnnaaa aaaaaccctg gaaaaccttt 1020  
 ggaaaaaaat tngnnggggg gccnttttgt tgggggggtt tnaaaaaacc ccctnggggg 1080  
 ttttttaagc ccaaaaagg gggaggggna aaangtnc cttntttttt ttttnngccc 1140  
 cccttgggga atggnttant tcanggggcc c 1171

<210> 742  
 <211> 739  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(739)  
 <223> n=A,T,C or G

<400> 742  
 gntgtcnaaa aagcaggctg gtaccgggtcc ggaattcgcg gccgcgtcga cggcccttgg 60  
 tgccactagt tctttcattc ttcccncca tcaatcagt aactttttag cctactcaaa 120  
 gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatatca 180  
 acatgaatat tttaaattaa ggcataagac atttttccta actgagcata gccatgaacc 240  
 tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaaagt 300  
 ccaggcagt cacaggtctt gacatgatga agtgacgtgt tgctatggtg attttgagc 360  
 tggccaaata gtcactggtt gattttaccc agcaggagat ttttgcaaaa atttcctggg 420  
 tgagagtga atcaaaactc tattttgtt ctcctctgca agctgnagtt aanatggatt 480  
 aatgagtact tttagattaa ttaactctga agagaaaaat ggagaaaagn gaggaaggtt 540  
 gttggcagaa gtcattgctg gaatccttct gaaggagta ctgaçttcac ttgcaaagac 600  
 aagagactan aagacaatga agttaaaactt ggcctgtctn tcatatgata gatgcttgag 660  
 agtacaggnt cagggaattt ttaattctgn catacgcata ttggattatg tgggtcatgg 720  
 ctttgtttgg cncctaacc 739

272

<210> 743  
<211> 610  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(610)  
<223> n=A,T,C or G

<400> 743  
ctgtcccttat ttcttttagca aaaatttccc aagagaagaa ttgctgggat aatgcacatt 60  
taaatttttg atagacattc ccaaataatta tacctgtttt tgagaccttt aattcctgtt 120  
gtcaaattgc cctatatatg gagtaataaa cacgatttaa agaaatgagg actaaaaaaa 180  
gattatatat aaccaacat aaaggcaacc tcttaggcgt tgacagaaac tgacaacttt 240  
ttatctgtgg gtgcgatcca ttataagtaa cctgagcacc ttattttttc tttttaaact 300  
ctaggttagga tacccgaggt ccacaaattt ttcataagaa atattttttc totgccctat 360  
gagattttta aaaatattat actgcttcaa ttgcatcaaa agaaatggac cctaatatct 420  
atgatgaagg atttggagtt agaagacctg agtttcaatt ttggcatggc tgtttgtcta 480  
gctctgngat cttggacagg tcaattgact tggcttaatc ttctcatcca tttagnggag 540  
acagcaccac tattcacagg actattgncn gaattaccag acaatagcat agnggaaaat 600  
ataangcctt 610

<210> 744  
<211> 127  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(127)  
<223> n=A,T,C or G

<400> 744  
ttnacctccc tggaccgggc ccccttccc cgggcggntc ccccgggctg caggaattct 60  
gcacgaggga gagagagttt gagagagaga gagagagaga gagagagaga gagananaga 120  
gagagag 127

<210> 745  
<211> 458  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(458)  
<223> n=A,T,C or G

<400> 745  
gatatcccgg gattcgcggc cgcgtcgacg tggcctctag tttgtcctgg tccaaagcag 60  
ggaagctggg ctacgtcctg ccaggtcag ccttaggtta agggctgcct gggggaggga 120  
acttcctggg ccttcgggtc tctgtgcact ggggtggctc ctgtggcca gaatgccctg 180  
gagaagggtc ctactggaag cgaagggtgca gggcagcagg gcctgaggcg caggagctgg 240  
tggaggctcc cagcacaggt cgccgcccc gtcacatcac tgctgatggg ggggggactt 300  
ggggagtttc ccccgagaat gggaggtctc acagtccccg tgctgcaatg ctgtcgggtg 360  
actgngncng caatgtgtc atggncaact gctttttctc tgtggccccg gccgatttat 420  
ccagcanngc acccctcttc tncctccgg anaaagcc 458

273

<210> 746  
<211> 893  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(893)  
<223> n=A,T,C or G

<400> 746  
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gaccccgctca tagagtaagt catcgataga gcatttgctt gatggggact tccagaaggc 120  
cannгааagt cctgccgact tcctggggaa gcccatccgc acgtgggggtg aggggtcccca 180  
natggaagca gctgtgtatg cagggagggg gcagaggctg ctgccaatgg gcatgtccct 240  
tacctgaaag ggccacctct ccagggtgaca tgtcctgggg gagccggggc cgtctgctcc 300  
ggccagaggc gctcagctca ggccacacca ggcagggcac ctcccaacct ggacagggtg 360  
ggaccaagggt ggcttggtac aaaactctct gtgtttgcc aacacccaat cggacacaga 420  
gagtcaacca caccacagtc acatgggtgc cacacngcag gggtaagga ggcccgggcc 480  
ctccccctca gacgtccctg ggcctctggg agtcagcaag gacgaggacg gcattgccct 540  
tcgagacagg aaggggagtga cctcctcccg gcggcatcca ggctcngctt ctccggagag 600  
gagagggggc tacttgctgg ataaancggc cggggccaca gagaaaaagc aaggtgacca 660  
tgagcacttt gaaacacag tgcacccacc agcatttnag caccngggac tgtgaagacc 720  
tcccatttct tcggggggaa acncgcccaa ngttccccc accntcacta gtgnattgtg 780  
acctgggggn cgggcccagc cctgtngctt gggnnagccc tccnccaggg tttctnnggc 840  
ngcccnttaa ngncacctng nttggccctt tggccnccct tncgcttttc cca 893

<210> 747  
<211> 738  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(738)  
<223> n=A,T,C or G

<400> 747  
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ggcagactgc catttgtcat tnattactga aggaaaggga tcctcagttt gcttggggac 120  
atttcaaatt tgagggtgaga gttggataag taagaataaa gctgctcttc aaagagatga 180  
atatagaaaa agaaacaaga tacagncttg gcagtaaggc tgggaggaag gggaaaagg 240  
aataaagaat gaaagagtga gaaatgtgag caggagctga acacagaaaa gttcagngac 300  
agaagcnaaa ggagggaaga agggaggagg gtccctttca cagaggctca cgaggatgct 360  
ttatgngtgc catgcagtcc atgttcagga tgtctgcttc ttanctctct acttttctaa 420  
tanaaatttg gatacttact gatcctacat atgtaacagg gagagaagggt gaatttcaa 480  
gcantaaatt gaaaaattgt tcacaatttc attttttaa aaaagggagc taacagaaga 540  
agagggttaat gtggttaatta taggatgnet cttgcgacac atgaatgnat ctggtatcat 600  
ctgagtgagg ggggagctgt cttcctgacc caaaaggatc ctttcgttan ccngnactta 660  
ngtcccaaaa cctcaccacc ttggagaaat natttccttt tgggggnttc attaaancct 720  
tttgnccccc gcaaaagc 738

<210> 748  
<211> 647  
<212> DNA  
<213> Homo sapiens

<220>



274

<221> misc\_feature  
 <222> (1)...(647)  
 <223> n=A,T,C or G

<400> 748  
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 agggcctctg tctccgctgc gctcgcctaa attggtatgg ctcgacttgg aaacacggtt 180  
 ctaacacgcg ttgttagcgc ccttgctagc atgtgaagga cactggccct accaagaaa 240  
 attcgagtcg ctccttccgg tatcggtcac ggagcgata tttactcttc ttactacggt 300  
 tacttcgaga ttgtctgtga agtttaagac tactaaaaag agtattaagc ctatcgggaa 360  
 ttagctagat cgacacgcta aaaccaaggg caatcgcgcg aaatatagag gcaccaataa 420  
 tagggcctac agaaggcccg agggtagac tcacgtttta taccggccac gggagaaaata 480  
 aaaagataaa gtatacatcg tttagcggtc ctcggaagcc ttcggcttta atgccaagga 540  
 gtcggaagca tcgtcgcgca gtaataaact ccatcgcgcc gagactatct acgacgccct 600  
 ccttaanac cgtaaattac tcccggaaa agtatttagg cggctct 647

<210> 749  
 <211> 642  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(642)  
 <223> n=A,T,C or G

<400> 749  
 cntgtggcg gtggntgtct catttgggtg gacttttttg gtcgtaggaa cctgggatgc 60  
 aggtccgcg agcgtgggct ctcgtcgtgg atgttggggg ttgggtgtgt gccggttgtt 120  
 tttggttctg ttgagcgtag tgtgtttgaa ggtagcggt cgtgtcttgc ttgtggtttg 180  
 gtgtttaggg cgggtgggga ggtgtgtgtg tagctgttgt atgtcatatt gttggtgttg 240  
 ctgccctgtg ctgtttgtcc ttggttattg tgggtgttac cccgcctgtg tggaggtgtt 300  
 gtggcagggc gggaatttaa gtgggagagt tgtgggaccc gtggtgtgtt ttacgttgc 360  
 gcttttgcg tgggcggtgg cggcgcgctc gataattaga attggatacg gagtgtataa 420  
 tacttctagt aaatggggac ctagtgcctg acttcccga ataggatct atgcgaagtc 480  
 cttagatag tctttgataa gtttaacgcc caccacccta aaattataca cgattagacg 540  
 cataacgact cctccaggaa agataaagaa tctcacatat agaacgggac cccatacacg 600  
 tcgtagatga aacaagagaa ctaattttng ttaaaaagac tt 642

<210> 750  
 <211> 639  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(639)  
 <223> n=A,T,C or G

<400> 750  
 tttgtggcgg ttgtgtctca tttgggtgga tttttgggtc gtaggtaacc tggatatngag 60  
 gtatagatgc cgattgggtcc cgacgagcgt caccgataaat tcggtagttt cggccttttt 120  
 agaaggcgct agtactcgga acttcacttc atctcggtag tttacttttg cgtatatagc 180  
 cttctccctc gaagactagc cgtcacattc gttccctagc aatcgtttct gcccttaaga 240  
 atccgagagc gagatcccga aactagagga accttagaag agtcgtattt ccacaaggac 300  
 cccacagtca ttccgggaaa atccctagga ccatacggtt aggattcccc cggaaccggg 360  
 agcaaagctc atgatttccc acaccgcgag agcgcctata accctatccc atttcttcgg 420

275

gttatcgagg atattacgat caagccgaga gaaccgctag aaccgctttc ttcgctttct 480  
cacggaacct ataagtagaa agagaaactc aggtcttaag gggcgcttc ggctaacgaa 540  
acttctactt acgaagagag tatctagaca ttaagtcata aaaatccact acgcacctcg 600  
tgtacgatat catcgggagc gggtcataga cggtgtccg 639

<210> 751  
<211> 637  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(637)  
<223> n=A,T,C or G

<400> 751  
cttttgtggc gngngtgtct catttgggtg gatTTTTTggg tcgtaggnaa cctggtatng 60  
aggcagctct gagccccccc ccccccccc cccccnccc ccccccccta gngngttggg 120  
aanacgggtg atacctaaat cgagtnggtt cattaaaagt agttgattac nccctaaaat 180  
aanaanaggc cttcgtcggg anaaatcggg aagganaagt cttnttggca tcataanaat 240  
actggctcgg gtcctaanat nttaaaggng gtcnccgagg gtnttcatac cgataanaaa 300  
cgTTTTccta tcggcaacgg gcttacctga gggnggactt ctncggngc gnggattnan 360  
acgaanacgt agaggattnc cgntacttnt tganatcacn cgtatcatac ttgtaagcat 420  
aattntcctg aaaagtgtta taanaatacg cncgcattat cgctTTTTcg tcctagggat 480  
gcttaaatgg cgatactgct atagcgggtg agcgttgggt ctcgagnaana aaagcgtgtc 540  
ctaatacgct taagnttta agnncgttgg tttaaaaata nccttagaaa cctcgaggcg 600  
gatactgggt tntttttaac gaaacaaagc accccnn 637

<210> 752  
<211> 644  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(644)  
<223> n=A,T,C or G

<400> 752  
tntgtggcgg tgggtctcat ttgggtggat ttttgggtcg taggaacctg gtatgaggtc 60  
ttgcgagttg ttggtgtgtc ctgtcgttcg gtggttcctt tttgagttga gtttgcctt 120  
tgaggttgtt agctgctgtt cgtttgtgtt cgtgtagtgc tttgggttga gagggttatg 180  
gtggtgggta cggtgtattg tcgcccgtgg tcgcccgggtt ggggtggtcg tcggttttgt 240  
ggttcatagt agtcttctgc gttcggtggt gcgggtttgg gtgagtagtt tcgttcttgg 300  
atgtcccat gaccgccat aatctaagta agggtagta gaaacctctc cccgatagac 360  
acaaccgtcg tccactaaag acctcgctc tgatttttaa aaggaccgga aaaacatccc 420  
ttcaacggaa aaaacggaaa aaaagtcagc gaattcaaag aagccacggg agagaaaaaa 480  
gaactaaagt tagtccgtca ttatatgtct cctcgaggga ggaagcggcg gtggcgga 540  
atgaggcggc aagaaagacg acctctatcg gcggcttang ccctaaaagg gcgatacctt 600  
acgggatgat aaggacccta ggacgcctcc ttctcgatc gtcc 644

<210> 753  
<211> 635  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature

276

&lt;222&gt; (1)...(635)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 753

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ctttgtggcg gtggtgctca tttgggtgga tttttgggtc gtaggaacct ggtatgaggg 60
aatcagctcg accccccccc cccccccct ccgaagcaga gcccaacca aagtccaccg 120
actacccgag taaactctcg gagggtagaa taagaaggag taggtcctag ccaatagaag 180
tagttccgag ccgttaggac agcggacgga acattnaaga aagagcctat attagggagg 240
aagtaacggt cctctttcgg agctctttaa ggggtagtcc cagaacaagg gaagaggacc 300
cgtcggctat tgcccgtcga tacgggctct cacgngagc ctaggttcga ggatagggcc 360
gctcgtaaaa ttatacggtt tccgagaaac gcttcgtag accgggtcct aaatcgtccg 420
gagtattngg agagggatcc ttcggaccct agggacagag agaggagaac ggaggttaca 480
ggaggagAAC gtntcctcnc tagttttctt tangtcgaaa aatttcttac cgataggggtt 540
cctagggtcg gngaatttac ggttcgaaaa acggtagtnc ctaangngtg ntattngggg 600
tagtatcggg tcgtttacaa ntogtccgtc ttntg 635

```

&lt;210&gt; 754

&lt;211&gt; 721

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(721)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 754

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accggtatng ttncgtgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattgtt ctgcnngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gtttttagt ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360
cccctaaagc agaggagaa taaggagttc tccccatgat ggaaaaatc caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc ttgcttctt cccacccctc ttcccagct ctctctctgt 540
ctctctcttg ntccccgtac ccttttttct tcccantgca tacttttttn ttccctttt 600
ttaatctct atantcttaa ncctaccaan gggcoctcnt gannaatttn tcacccctga 660
ataggggatt ctntangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720
a 721

```

&lt;210&gt; 755

&lt;211&gt; 721

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(721)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 755

```

accggtatng ttncgtgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattgtt ctgcnngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gtttttagt ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300
atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360

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277

```

cccctaaagc agagggagaa taaggagttc tcccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc ttgtcttctt cccaccctc ttcccagct ctctctctgt 540
ctctctcttg ntcccctgac ccttttttct tcccantgca tacttttttn tttccctttt 600
ttaatcttct atantcttaa ncctaccaan gggccctcnt gannaatttn tcaccctga 660
ataggggatt cntangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720
a                                                                                   721

```

```

<210> 756
<211> 873
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(873)
<223> n=A,T,C or G

```

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<400> 756
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ggaaactgtc agcctgtctc tttcactttg ggcaagtga agcaaagacg tccagtccta 120
tcagcaatta ggctgaaagt caacgccaaag ctggcgggca agggctggtc tgagtagagg 180
ttccctaggg aggcaagaga gagactccca ctcgatactc ccagctcggc aactgcctga 240
atgccaatga gcactcatta taaccgcccc tattttatag gatttaattt tacacttcag 300
gcttaatcag tctgaaagtt aaactgacag tgtaagttta cggaatcaat gacatttagg 360
ctttatgact ttgtagctga atatctatgg gctatatttc cattctaaca gtgatatact 420
gttccagaat ctcatctctt ggtgatggca ctttctagtg gagcagtcac ggtaacagtc 480
cacacccatt accatgtggg tgctttacag catactgacg gaaggactga ggagccaccg 540
gagcaggagt tctctcaggg gaggacgctg acacttccac agctgcctan gtatgggcac 600
ctgatgccaa cgaanaaccc aaagcgctct cccttccaga tggaagctgc cccacactgg 660
gctgacagca tctggagctg ctctggctca aatcccgga tgcacacnct cctancgggg 720
gcgtttanag atcctcnggg ccagctaccg accactttg acaagggnc ttaggagcga 780
aactagnctg gcgcgttaca cncggatgga acgtcttgg cttgagacct cttgggggan 840
atggcncccc caaataantt gggaaaaantn ggg                                                                                   873

```

```

<210> 757
<211> 782
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(782)
<223> n=A,T,C or G

```

```

<400> 757
ggcccctcga gggatactct agagcggccg ccgactagt agctcgtcga cgatatcccc 60
ggatttgaga ccaggagaca gctccagatg ctgtcagccc agtgcggtgg gcaggcttcc 120
atctgtgaag tggagaggcg ctttgggctt ctctgttggc atcaggtgcc catacctagg 180
gcagctgttg aagtgtcagc gtcctccctg agaggaactc ctgctccggt ggctcctcag 240
tccttcctgc agtatgctgt aaagcaccga catggtaatg ggtgnggact ggtaccatga 300
ctgntccctt aaaagggtggc cttccnaag aaaggagaat tcttggacna gggatttcac 360
ttgnttagaa atgggaaaaa ttaccatta gaattttcgn ttccaaggcn tnaagnccta 420
aaaggccttt gattcccgaa ccttaaccct gggcagttaa cttttcaaac gggataaacc 480
ctgangggga aaatnaaatc ctttaaaaaa gggggggttt naaggagggc tctttggctt 540
tcaggcantt gccaacctgg gaaattcana ggggaagtnt tttttttg ctcgctaggg 600
aacctttact taaacnaacc cttgncccc ctttggggt tgactttcan cctaattgct 660
gaaaggaccg ggccgntttt gntttccttt gncccaaagg naaanaaacg ggtgccantt 720

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278

cccangggat tanttcccgaa aattttggnn aatttttntt tgnactttt tgggtttttt 780  
cc 782

<210> 758  
<211> 647  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n=A,T,C or G

<400> 758  
ntttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60  
gggaagagcg ccgtcgggtcc gactacagta tggagtagta tagtcttcgc gccttctcgg 120  
gcggcggggc tattctctcc aaaggcagag gtccctagtc gacctcgtc ccctagggtta 180  
ggaacagccg tcgaatatct taggttcgtc gaggttttct tccgagctct acgcctaagt 240  
agctccgcga gaaagtatc ggtcattttc ccctatccat cactccccta agtacgcctc 300  
attattccgg aaggcaagag gccagcattc ctcccttagag tagagggtag gtacctccgt 360  
cgcggtccgc gaaagggcag agcttcgtgt cttccctccg cagcagctta acgggtctacg 420  
taggcgttct cgatcttttc acgggaatcg gggccgggga gggcggcgga aaacgtcgac 480  
gtctcgggtca ccgtcaccgc cccgaacaac tagcggcttt ccgctttcaa ctgaggaacc 540  
ccgcacccct cattagcgct tacgaaatcg gggangtgat tgcgccaat cgttagcctt 600  
cgataattat tctctattag cgttcctatc tcgcgctttc gatttat 647

<210> 759  
<211> 657  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(657)  
<223> n=A,T,C or G

<400> 759  
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60  
gggtctctata gaaagcctct tgtcttttaga tacgggcttt ctggtccttc gttctggaag 120  
tgtagtagta ggtactgcgg gaaggcgaag agtcctttca aggacgattt acttaagttg 180  
gcttattcta tagttccttc gggacataag gtcggtagca tctatactgc gtgggaagct 240  
gataggttgg gacttaaggc gaataagaag gaggcggcgg aggtcgcgat taccgcagag 300  
atattattta cggcgccgcg ggtaccgcg ggtcatgcgg aaattttctg aggttcttgg 360  
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accggtacaa actcaagaag aagttcccat taagcatcgt aagaaacggg aggacgagga 480  
cggttaagaag taatcggaga aaggatccta gtngttacga agaagcatcg ttnagctact 540  
ttgcgctacc gtttatattt agacgtgttc cgtccttctc cgtgtttana aaaaaggttt 600  
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<210> 760  
<211> 644  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(644)  
<223> n=A,T,C or G

279

&lt;400&gt; 760

```

ctttgtggcg gtggtgtctc atttgggtgg acttttttggg tcgtaggaac ctggtatgna 60
ggaaaagaag taagcctcga agcctatctc cgaccgtatt tatttcgcag aagacggaac 120
tacggacgtc gtttaaccccg agtagccccc gtaagaaagg actaaagcga atggaaaagt 180
cggaattcc ggcgagggg cgcgattac tgaaggagt aagagtaaga ctattgcgat 240
acttgaggcg ttccctctta aaaggcacc gaaacactct attaaaaaac acccgaagaa 300
gaacaactca tgcgatcggc cgtgtgcagc cgtcaatagt aaagagagcc atgaaccatg 360
ccatccttag accaattagg atgaagaaga ggaggaagat gaggaccaa ccctaccac 420
tcggaaaacc ccgcacgagc ctccgaacaa aatccgggaa ttaaaacggc ggcccacttc 480
cgactctcg tagcgcgagc cgaatagaaa accggaaact acagctaaag ggtcctttcc 540
ggcctgttat ctaccacccc gcaatccgat cctccccccc cctcgtccaa aaaccctaac 600
ctctgcggca acattagagc agaaggagag ggcgatccct tgan 644

```

&lt;210&gt; 761

&lt;211&gt; 647

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(647)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 761

```

ctttgtggcg gtggtgtctc atttgggtgg acttttttggg tcgtaggaac ctggtatnga 60
ggcgggtact ctctgggata atcgggtataa gtgttgtaaa attgggggta agagaaagt 120
tcattataag aagtggagc acgagccggg gtgttttagtc gttaatatta agaccggtt 180
ttgttgact tatatagctt gcgcgtggg aggcaataag aaacattgcg ttctgagggc 240
ggatgcgggg aacctcttc ggggtctaga gcgcgcgcat tgcaaaataa ggactactga 300
cgccgctcat aacgtactca acaatgagtc ggcctgcatt aagatttcg cgaagaaccg 360
tactgcgtct actgatagta tattgcattg atagcggcat gagctttatc acgtgtcgtt 420
ttcgggttgt aagaaggag ttaagtcgat cttcgaggaa gaagagaccc caaataaaaa 480
atgactcaaa aaaacctaga agaaacacga cgaaggaaa aagaacgta aaactagtag 540
ctctcggan gagtagcctt agtagggtaa gtcctccgtg cgtactgtcc taaggtttg 600
atagcgggt tgaatagacg gtcacgcgtc agaaggtaaa aancgg 647

```

&lt;210&gt; 762

&lt;211&gt; 628

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(628)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 762

```

cattgtgttg ggtcactga gccactttt ttccagattt tttgtaaaat tgtttcgcat 60
tgtgttccct ttattcgctt gtattaatat ttgcgtagt gattaaacaa atacttggtg 120
ttgactgtca gtcttagagg actgactaga agtagtttct atttggggct caggaaatac 180
ctactttata tttctagcta attaggaaag tcatttttca gttaggtttg tgttttggtt 240
caggcactcg ctagctagat gacctaacat gctacttaat ttctgagtgt ttgtgtccat 300
ccctgtagga ttgttcggg gttaaatgaa attgtgtata tttgtaaagc atttacctca 360
gtgcccagac tgtgacagag tagattatta ggcttgctct tatttctgtg attaaattta 420
gtgtcagatt agcaacctat agctacttct aaagctgctg ctgctttctt tgtttagggt 480
taggaagaaa catgctggac agtttgccaa atgagagtta catgatgttg cttgtgggaa 540
cattctaact tggaacttgc ccatttccag gactttgnng ttcanagatt tttggggata 600

```

gatgtaaggg ttaaaaaaaaa cngaaaac

628

<210> 763  
<211> 147  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(147)  
<223> n=A,T,C or G

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gaaaagctaa ctggataact tacagcatgt ttctgccaat aatctcttan aacaggcctc 120  
ttttttttat gcacaccacc ttcnggc 147

<210> 764  
<211> 146  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(146)  
<223> n=A,T,C or G

<400> 764  
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nnnaactggg gccgnntgct cagtat 146

<210> 765  
<211> 129  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(129)  
<223> n=A,T,C or G

<400> 765  
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ccagtgtggg nggaattcca ttgtgttggg gcaggaggng ctttgngtac ngtgcggctg 120  
nagaggcgg 129

<210> 766  
<211> 175  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(175)  
<223> n=A,T,C or G

<400> 766

281

cattgtgttg ggcctagtc gaatactttt agtaacttca gacagatctc ctcattctctt 60  
tctggggcctt ggnnttttctc ctttgtanaa tgatgccttt ctgtgggttt gtcatttcta 120  
acattctgtg ngtgatgagg tgtatatctg anganctcta tcncanagt actct 175

<210> 767  
<211> 602  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(602)  
<223> n=A,T,C or G

<400> 767  
nnntttaaaa nctgtntctc ccgcgggtggc ggccgctcta gaactagtgg atcctttcca 60  
cctggtttgt tttcagtgtt taatcctatt agtatcagca ggatataggt caggatatca 120  
ggtgcagaac ctgtggaatc agccaatttg gcttgctcat ttactttaat aaggteccat 180  
aatgagttag agtacaaagt tcaagccctg ttgagggtct gcattaaact ctcagaagta 240  
tttagagtgt gccaggagcc gcgaaggctt ggttcgggtg gtggcgggaa ctgtattaga 300  
gtgctaggca cggcgcgaca aagtctgtcc aaccctaaac ggtgctgagg cgttgggtgt 360  
gagctccagt actcagaaaa gcatctcagc aggtactcaa cagatcctca ggggcttggg 420  
ggcccagcac tggcagttag ggcagtaaag acataaaagg gcactacctg tgggtatttt 480  
ctgttctcca aggaggaggt agcaaaaatt aggacgctgg aatatcctat gttgtagcaa 540  
tcccagaaca actgatgctc aaacaatacc acacaaaaca aattttttaa aatttaattct 600  
ta 602

<210> 768  
<211> 671  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(671)  
<223> n=A,T,C or G

<400> 768  
tccaccgcgg tggcggccgc tctagactag tggatccact agtccagtgt ggggtgggaat 60  
tcgcggcneg cgtcgacaaa aatactgcta aagtaatat tttatagatg actatttgcc 120  
ttggggccag gaaaagcagc tggagttatt cacttagtac catttttaca tactaacttt 180  
gccttttcca tgcttgcttg atgcggcttg cagcactgaa gaacagtttc aattgctagc 240  
caaccagaga gcatgatcaa accaaacaag ttccctgttt caggaaaaac aggttttagg 300  
taactgaagg gttaccagtt actgattcca caatcttctc tgtaaaanat ttctgcctat 360  
tatgcagact gggcggtttt aaanntggtt aaactatnaa ataccatac aatattttaa 420  
nggggcccnn ttatnaagct tttcaggcct tcccctttcc atagcattgg tgggatacaa 480  
gaaaccttta aacagcaacn agctatcnag gcccataaag aaagtaattt tgatttttta 540  
nagattccgn aacgaaaaaa tggctgggtt caaatacnac cttcttttta aaatggnntc 600  
cttattaaac nttttttttt ttttaattta ccccatggtc ntgatnttng ngcttccgcc 660  
canaaaatng n 671

<210> 769  
<211> 877  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature



&lt;222&gt; (1)...(877)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 769

```
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ngggggaatt cgcggccgcg tcgacctcta tacctttgnt catgcagctt cctctgactg 120
ggtttgttct tcacttggct aacccctctt ttacttaagc acaccttgaa cattccctcc 180
ttccccattt ccccgacng cccctaattg acatacttct gaataacaca ggtggtattc 240
cttccttgtt ggaacctcct ggaggaagag acagatgatt aacaaatcct tccatcaacc 300
cctttgacca tgacatcaac agtgctccaa attatggggt accgtattag cctatgtcta 360
tcttgatcag aatccttacc tcggtgtatt gaaattatct atttcgtgcc tgcctcttta 420
aagtccagggt ttgccttacc tattgtctaa caccatgcag taggtaacat gcagtaggaa 480
acatggcatt aaattatttt ggttcaaata ccagttatgg tgtgtaaatg cctaccaggc 540
cgtgaggcac ctgctaagca ggttgacgc atcatttgaa ttcacaccac ccttttgcaa 600
tagaacagat aggcaacaga ggctcatttg ggctaaagga tttgatggag gggaaagtgc 660
aggattccca ccaaggcctc anggccagg tccanggacc atgtctgttg tgacaactgg 720
agtgcatttc atatccctn ctctgngggg naaggctccct cncgnggaga acnnttaaaa 780
caatcatntc tnggggngnt aatgcttctt nccccagtg gttnccactgc ngccacgagt 840
cccancact agtcccangt ctgtcatgaa ccancec 877
```

&lt;210&gt; 770

&lt;211&gt; 874

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(874)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 770

```
ctggnctccc cgcggtggcg gccgctctag aactagtgga tccactagtc cagtgtggtg 60
gaattcgcgg cgcgctcgac cttttcaaag gttacttat ttaattatca canngcaac 120
ccgatgagta ggtaacagta ttttactgat aggtaatcta aagaaggagg ctaaataaat 180
tgcccaattt cgaacagtga gaggaagaat taggattgaa acacatatag tggcttcaga 240
atctgtaacc ctacagatgc cactactact tctttcagaa taccctttgc ctatctattc 300
tgttctatg tcatcaaatt atacttactt taaaaagtat ttgtctttat tttttttaa 360
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ttttgagggt ttctcccttg ccagtttttc tatgctgggt tattcaagtc ctaagaattg 480
tgtagctatt acagaaccgc tttagcaaat gtgtccatt aatcaagggt atttataaca 540
aaatttcac caagtttgga gtgctctgaa aacatagcca aaatgttcgc agggcttacc 600
cctctcgtgt gtcccttttt tttagctatt tcagaagcac actggtgcaa ttttttacga 660
aatgagtttc ttccctttac ctctgcatcc tctaagaaaa aatcattgnt gttttatgaa 720
natgaanatc ctgctatttc atatcttgat tggagctgct taattaaatg accatttttna 780
aatttgtttt gattccnngc aaaaaaagtt tnttnttgga tgtagggggc tcnnaaagnc 840
caaaaccccc caaaattttt nnttgggaac ccna 874
```

&lt;210&gt; 771

&lt;211&gt; 156

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(156)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 771

283

```

ttaaaaaanct ggncctccccg cgggtggcggc cgctctagaa ctagtggatc cactagtcca 60
gtgtggtgga attcgcggcc gcgtcgaccg cgagcggctg ccctttttt ttttttttn 120
ngtttttttg aanaattcat tgggtattta ttattc 156

```

```

<210> 772
<211> 586
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(586)
<223> n=A,T,C or G

```

```

<400> 772
ncaanctggn ctccaccgcg gtggcggccg ctctagacta gtggatccac tagtccagtg 60
tggtggaatt cgcgcccgcg tcgatcacaa agtgctcaca agtccngnat ttattttatc 120
tccagatatg aaacttaccc ccagctatgg tcttctatgt gttatttaat ttctaggcca 180
attttttcca cttgaatgtc agtattttta ttcaaagtca ccttgccaa ataccaagtc 240
atcaacttac cctcaaatga tatcctcatt cagaaaatct acatctatta atggtagcta 300
ttttatccct gccccctgct ttttcttttt atatttaatt aatttgntca tccagcaaat 360
gcttattgag caggtattgt aggctaaaca attctanact ttaaggggac acagnttgca 420
aaacaaaatc ctgccttgna tggatactta tgnnatggng ggatacagac aatcaacata 480
atgangngca tcatatataa tggttagnan aatgataagg gnttttggga aaaaaatgca 540
cccancnaan anggattggg aagtggangg ganggtcang ggangg 586

```

```

<210> 773
<211> 2983
<212> DNA
<213> Homo sapiens

```

```

<400> 773
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aagagctgca agttctccac attgacttct tgaatcagga caacgcggtt tctcaccaca 120
catgggagtt ccaaaccgagc agtcctgtgt tccggcgagg acaggtgttt cacctgcggc 180
tggtgctgaa ccagccccta caatcctacc accaactgaa actggaattc agcacagggc 240
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ccagttcccc caatgccatc ctgggcaagt accaactaaa cgtgaaaact ggaaaccaca 420
tccttaagtc tgaagaaaac atcctatacc ttctcttcaa cccatgggtg aaagaggaca 480
tggttttcat gcctgatgag gacgagcgca aagagtacat cctcaatgac acgggctgcc 540
attacgtggg ggctgccaga agtatcaaag gcaaaccctg gaactttggt cagtttgaga 600
aaaatgtcct ggactgctgc atttccctgc tgactgagag ctccctcaag cccacagata 660
ggagggaccg cgtgctgggtg tgcagggcca tgtgtgctat gatgagcttt gagaaaggcc 720
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tgggccaaga caggcggaga gatcacct atgagtacaa gtatccagaa ggctcctctg 1380
aggagaggca ggtcatggat catgccttcc tcttctcag ttctgagagg gagcacagac 1440
gacctgtaaa agagaacttt cttcacatgt cgttacaatc agatgatgtg ctgctgggaa 1500

```

```

actctgttaa tttcacctg attcttaaaa ggaagaccgc tgcctacag aatgtcaaca 1560
tcttgggctc ctttgaacta cagttgtaca ctggcaagaa gatggcaaaa ctgtgtgacc 1620
tcaataagac ctgcagatc caaggtcaag tatcagaagt gactctgacc ttggactcca 1680
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```

&lt;210&gt; 774

&lt;211&gt; 3064

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 774

```

aattctaaaa atgcttttgc aagcttgcac gcctgcaggt gcagcggccg ccagtgtgat 60
ggatatctgc agaattcggc ttgcgctcag ctggaattcc gcagagatag agtcttccct 120
ggcattgcag gagagaatct gaagggatga tggatgcac aaaagagctg caagtctctc 180
acattgactt cttgaatcag gacaacgccg tttctacca cacatgggag ttccaaacga 240
gcagtctgtg gttccggcgd ggacaggtgt ttcacctgcg gctggtgctg aaccagcccc 300
tacaatccta ccaccaactg aaactggaat tcagcacagg gccgaatcct agcatcgcca 360
aacacaccct ggtggtgctc gacccgagga cgccctcaga cactacaac tggcaggcaa 420
cccttcaaaa tgagtctggc aaagaggtca cagtggctgt caccagttcc cccaatgcca 480
tcctgggcaa gtaccaacta aacgtgaaaa ctggaaacca catccttaag tctgaagaaa 540
acatcctata ccttctcttc aaccatggt gtaaagagga catggttttc atgcctgatg 600
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gaagtatcaa atgcaaaccc tggaaacttg gtgagtttga gaaaaatgtc ctggactgct 720
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cgagaaaaat caccagtatg acccacgact ctgtctggaa ttccatgtg tggacggatg 1140
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<210> 775
<211> 684
<212> PRT
<213> Homo sapiens
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				5					10					15	
Asn	Gln	Asp	Asn	Ala	Val	Ser	His	His	Thr	Trp	Glu	Phe	Gln	Thr	Ser
			20					25					30		
Ser	Pro	Val	Phe	Arg	Arg	Gly	Gln	Val	Phe	His	Leu	Arg	Leu	Val	Leu
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Thr	Ala	Pro	Tyr	Lys	Trp	Thr	Gly	Ser	Ala	Pro	Ile	Leu	Gln	Gln	Tyr
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Tyr	Asn	Thr	Lys	Gln	Ala	Val	Cys	Phe	Gly	Gln	Cys	Trp	Val	Phe	Ala
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<210> 776  
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 <212> PRT  
 <213> Homo sapiens

<400> 776  
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 Asn Gln Pro Leu Gln Ser Tyr His Gln Leu Lys Leu Glu Phe Ser Thr  
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 Gly Pro Asn Pro Ser Ile Ala Lys His Thr Leu Val Val Leu Asp Pro  
 65 70 75 80  
 Arg Thr Pro Ser Asp His Tyr Asn Trp Gln Ala Thr Leu Gln Asn Glu  
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 Ser Gly Lys Glu Val Thr Val Ala Val Thr Ser Ser Pro Asn Ala Ile  
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288

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&lt;210&gt; 777

&lt;211&gt; 5668

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 777

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&lt;210&gt; 778

&lt;211&gt; 1095

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 778

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          20              25              30
Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
          35              40              45
Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
          50              55              60
Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
          65              70              75
Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
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Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
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His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
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 Glu Asp Ala Pro Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe  
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&lt;210&gt; 779

&lt;211&gt; 3639

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 779

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<211> 1095

<212> PRT

<213> Homo sapiens

<220>

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Gly	Tyr	Phe	Leu	Ala	Gln	Tyr	Leu	Met	Asp	Asp	Phe	Thr	Arg	Asp	Pro
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Leu	Tyr	Ile	Leu	Asp	Asn	Asn	His	Thr	His	Leu	Leu	Leu	Val	Asp	Asn
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295

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&lt;210&gt; 781

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 781

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 782

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298

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<210> 799  
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 <212> PRT  
 <213> Homo sapiens

<400> 799  
 Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu Ser Val Arg His  
                   5                  10                  15

<210> 800  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 800  
 Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu  
                   5                  10                  15

<210> 801  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 801  
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
                   5                  10                  15

<210> 802  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 802  
 Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu  
                   5                  10                  15

<210> 803  
 <211> 14  
 <212> PRT

300

&lt;213&gt; Homo sapiens

&lt;400&gt; 803

Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu  
5 10

&lt;210&gt; 804

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 804

Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
5 10 15

&lt;210&gt; 805

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 805

His Pro Gln Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser  
5 10 15

&lt;210&gt; 806

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 806

Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His  
5 10 15

&lt;210&gt; 807

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 807

Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val  
5 10 15

&lt;210&gt; 808

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 808

Ala Leu Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val  
5 10 15

&lt;210&gt; 809

301

<211> 17  
<212> PRT  
<213> Homo sapiens

<400> 809  
Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe Cys  
5 10 15

Ser

<210> 810  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 810  
Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu  
5 10 15

<210> 811  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 811  
Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser  
5 10 15

<210> 812  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 812  
Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser  
5 10 15

<210> 813  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 813  
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
5 10 15

<210> 814  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 814

<400>	817					
atgaggaaca	gaaggaatga	cactctggac	agcaccgcga	ccttgtactc	cagcgcgtct	60
cggagcacag	acttgtctta	cagtgaagc	gacttggtga	attttattca	agcaaatatt	120
aagaaacgag	aatgtgtctt	ctttaccaa	gattccaagg	ccacggagaa	tgtgtgcaag	180
tgtgtctatg	ccacagacca	gcacatggaa	ggcaccaga	tcaaccaaag	tgagaaatgg	240
aactacaaga	aacacaccaa	ggaatttctt	accgacgcct	ttggggatat	tcagtttgag	300
acactgggga	agaaggga	gtatatacgt	ctgtcctgcg	acacggacgc	ggaaatcctt	360
tacgagctgc	tgaccagca	ctggcaacctg	aaaacaccca	acctggctat	ttctgtgacc	420
gggggcgcca	agaactctgc	cctgaagccg	cgcattgcga	agatcttcag	ccggctcatc	480
tacatgcgcg	agtcacaaag	tgctgtgatt	ctcaccggag	gcaccattca	tggctgatg	540
aggtacatcg	ggggggtggt	gagagataac	accatcagca	ggagttcaga	ggagaatatt	600
gtggccattg	gcatagcagc	ttggggcatg	gtctccaacc	gggacaccct	catcaggaat	660
tgcatgtctg	agggtatttt	tttagcccag	taccttatgg	atgacttcac	aagagatcca	720
ctgtatatcc	tggacaacaa	ccacacacat	ttgtgtctcg	tggaacaatg	ctgtcatgga	780
catcccactg	tcgaagcaaa	gctccggaat	cagctagaga	agtatatctc	tgagcgcact	840
attcaagatt	ccaactatgg	ttggcaagtc	cccatttgtt	gttttgccca	aggagggtga	900
aaagagactt	tgaagccat	caatacctcc	atcaaaaata	aaattccttg	tgtggtgggtg	960
gaaggctcgg	gccagatcgc	tgatgtgatc	gctagcctgg	tggaggtgga	ggatgccctg	1020
acatctttctg	ccgtcaagga	gaagtgtggtg	cgctttttac	cccgcacggt	gtccccggtc	1080
cctgaggagg	agactgagag	ttggatcaaa	tggtctcaag	aaattctcga	atgttctcac	1140
ctattaacag	ttattaaaaat	ggaagaagct	gggatgaaa	ttgtgagcaa	tgcaatctcc	1200
tacgtctctat	acaaggcctt	cagcaccagt	gagcaagaca	aggataactg	gaatgggcag	1260
ctgaagcttc	tgctggagtg	gaaccagctg	gacttagcca	atgatgagat	tttccaacct	1320
gaccgcgat	gggagctctg	tgaccttcaa	gaagtcatgt	ttacgggtct	cataaaggac	1380
agaccacaagt	ttgtccgcct	ctttctggag	aatggcttga	acctacggaa	gtttctcacc	1440
catgatgtcc	ttaactgaact	ctttctcaac	cacttcaqca	cgttgtgtga	ccggaatctg	1500

<213> Homo sapiens

Met	Arg	Asn	Arg	Arg	Asn	Asp	Thr	Leu	Asp	Ser	Thr	Arg	Thr	Leu	Tyr
				5					10					15	
Ser	Ser	Ala	Ser	Arg	Ser	Thr	Asp	Leu	Ser	Tyr	Ser	Glu	Ser	Asp	Leu
		20						25				30			
Val	Asn	Phe	Ile	Gln	Ala	Asn	Phe	Lys	Lys	Arg	Glu	Cys	Val	Phe	Phe
		35					40				45				
Thr	Lys	Asp	Ser	Lys	Ala	Thr	Glu	Asn	Val	Cys	Lys	Cys	Gly	Tyr	Ala
	50				55					60					
Gln	Ser	Gln	His	Met	Glu	Gly	Thr	Gln	Ile	Asn	Gln	Ser	Glu	Lys	Trp
	65				70					75					80
Asn	Tyr	Lys	Lys	His	Thr	Lys	Glu	Phe	Pro	Thr	Asp	Ala	Phe	Gly	Asp
				85					90					95	
Ile	Gln	Phe	Glu	Thr	Leu	Gly	Lys	Lys	Gly	Lys	Tyr	Ile	Arg	Leu	Ser
		100						105					110		
Cys	Asp	Thr	Asp	Ala	Glu	Ile	Leu	Tyr	Glu	Leu	Leu	Thr	Gln	His	Trp
		115					120					125			
His	Leu	Lys	Thr	Pro	Asn	Leu	Val	Ile	Ser	Val	Thr	Gly	Gly	Ala	Lys
	130				135					140					
Asn	Phe	Ala	Leu	Lys	Pro	Arg	Met	Arg	Lys	Ile	Phe	Ser	Arg	Leu	Ile
	145				150					155					160
Tyr	Ile	Ala	Gln	Ser	Lys	Gly	Ala	Trp	Ile	Leu	Thr	Gly	Gly	Thr	His
			165					170						175	
Tyr	Gly	Leu	Met	Lys	Tyr	Ile	Gly	Glu	Val	Val	Arg	Asp	Asn	Thr	Ile
		180						185					190		
Ser	Arg	Ser	Ser	Glu	Glu	Asn	Ile	Val	Ala	Ile	Gly	Ile	Ala	Ala	Trp
		195					200					205			
Gly	Met	Val	Ser	Asn	Arg	Asp	Thr	Leu	Ile	Arg	Asn	Cys	Asp	Ala	Glu
	210					215					220				
Gly	Tyr	Phe	Leu	Ala	Gln	Tyr	Leu	Met	Asp	Asp	Phe	Thr	Arg	Asp	Pro
	225				230					235					240
Leu	Tyr	Ile	Leu	Asp	Asn	Asn	His	Thr	His	Leu	Leu	Leu	Val	Asp	Asn
			245					250						255	
Gly	Cys	His	Gly	His	Pro	Thr	Val	Glu	Ala	Lys	Leu	Arg	Asn	Gln	Leu
		260						265					270		
Glu	Lys	Tyr	Ile	Ser	Glu	Arg	Thr	Ile	Gln	Asp	Ser	Asn	Tyr	Gly	Gly
		275					280					285			
Lys	Ile	Pro	Ile	Val	Cys	Phe	Ala	Gln	Gly	Gly	Gly	Lys	Glu	Thr	Leu
	290					295					300				
Lys	Ala	Ile	Asn	Thr	Ser	Ile	Lys	Asn	Lys	Ile	Pro	Cys	Val	Val	Val
	305				310					315					320
Glu	Gly	Ser	Gly	Gln	Ile	Ala	Asp	Val	Ile	Ala	Ser	Leu	Val	Glu	Val
			325					330						335	
Glu	Asp	Ala	Leu	Thr	Ser	Ser	Ala	Val	Lys	Glu	Lys	Leu	Val	Arg	Phe

304

```

      340      345      350
Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
      355      360      365
Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
      370      375      380
Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385      390      395      400
Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
      405      410      415
Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
      420      425      430
Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
      435      440      445
Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
450      455      460
Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465      470      475      480
His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
      485      490      495
Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
500      505      510
Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
      515      520      525
Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
530      535      540
Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545      550      555      560
Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
      565      570      575
Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
580      585      590
Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
595      600      605
Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
610      615      620
Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625      630      635      640
Ala Trp Gly Gly Leu Glu His His His His His His
      645      650

```

&lt;210&gt; 819

&lt;211&gt; 132

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 819

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
1      5      10      15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
      20      25      30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
      35      40      45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
50      55      60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
65      70      75      80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala

```

305

										85			90			95		
Asp	Ala	Leu	Asn	Gly	His	His	Pro	Gly	Asp	Val	Ile	Ser	Val	Asn	Trp			
				100			105			110								
Gln	Thr	Lys	Ser	Gly	Gly	Thr	Arg	Thr	Gly	Asn	Val	Thr	Leu	Ala	Glu			
				115			120			125								
Gly	Pro	Pro	Ala															
130																		

```
<210> 820
<211> 36
<212> DNA
<213> Artificial Sequence.
```

<220>  
<223> PCR primer

<400> 820  
ggggaattca tgatccggga gaaatttgcc cactgc 36

```
<210> 821
<211> 33
<212> DNA
<213> Artificial Sequence
```

<220>  
<223> PCR primer

<400> 821  
gggctcgagt caggagtttg agaccagcct ggc 33

```
<210> 822
<211> 675
<212> DNA
<213> Homo sapiens
```

<400> 822							
atgcataacc	atcaccatca	cacggccgcg	tccgataaact	tccagctgtc	ccagggtggg	60	
cagggattcg	ccattccgat	cgggcaggcg	atggcgatcg	cgggccagat	caagcttccc	120	
accgttcata	ctcggcctac	cgccttctct	ggcttgggtg	ttgtcgacaa	caacggcacc	180	
ggcgacgag	tcacaacgct	ggtcgggagc	gctccggcgg	caagtctcgg	catctccacc	240	
ggcgacgtga	tcaccgcggt	cgacggcgct	ccgatcaact	cggccaccgc	gatggcggac	300	
gcgcttaacg	ggcatcatcc	cggtagcgtc	atctcgggtg	cctggcaaac	caagtcgggc	360	
ggcacgcgta	cagggaacgt	gacattggcc	gagggacccc	cggccgaatt	catgatccgg	420	
gagaaatttg	ccactgcac	cgtgctaacc	attgcacaca	gattgaacac	cattattgac	480	
agcgacaaga	taatggtttt	agattcagga	agactgaaag	aatatgatga	gccgtatggt	540	
ttgtgc meta	ataaagagag	cctattttac	aagatgggtc	aacaactggg	caaggcagaa	600	
gccgtgcgcc	tcactgaaac	agcaaaacag	agatgggggt	tcaccatggt	ggccaggctg	660	
gtctcaaaat	cctga					675	

```
<210> 823
<211> 291
<212> DNA
<213> Homo sapiens
```



306

&lt;400&gt; 823

```

atggggatcc gggagaaatt tgccactgc accgtgctaa ccattgcaca cagattgaac 60
accattattg acagcgacaa gataatggtt ttagattcag gaagactgaa agaatatgat 120
gagccgtatg ttttctgca aaataaagag agcctathtt acaagatggt gcaacaactg 180
ggcaaggcag aagccgctgc cctcactgaa acagcaaaac agagatgggg tttcaccatg 240
ttggccaggc tgggtctcaa ctcctcagag caccaccacc accaccactg a 291

```

&lt;210&gt; 824

&lt;211&gt; 1074

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 824

```

atgtcagcca ttgagagggt gtcagaggca atcgtcagca tccgaagaat ccagaccttt 60
ttgtactttg atgagatatc acagcgcaac cgtcagctgc cgtcagatgg taaaaagatg 120
gtgcatgtgc aggattttac tgctttttgg gataaggcat cagagacccc aactctacaa 180
ggcctttcct ttactgtcag acctggcgaa ttgttagctg tggtcggccc cgtggggagca 240
gggaagtcac cactgttaag tgccgtgctc gggaattgg cccaagtca cgggctgggc 300
agcgtgcatg gaagaattgc ctatgtgtct cagcagccct ggggtgttctc gggaactctg 360
aggagtaata ttttatttgg gaagaaatac gaaaaggaaac gatatgaaaa agtcataaag 420
gcttgtgctc tgaaaaagga tttacagctg ttggaggatg gtgatctgac tgtgatagga 480
gatcggggaa ccacgtgtag tggagggcag aaagcacggg taaaccttgc aagagcagtg 540
tatcaagatg ctgacatcta tctcctggac gatccttca gtgcagtaga tgcggaagtt 600
agcagacact tgttcgaact gtgtatttgc caaathttgc atgagaagat cacaatttta 660
gtgactcacc agttgcagta cctcaaagct gcaagtcaga ttctgatatt gaaagatggt 720
aaaatggtgc agaaggggac ttacactgag ttcttaaaat ctggtataga ttttggctcc 780
cttttaaaga aggataatga ggaaagtga caacctccag ttccaggaac tcccacacta 840
aggaatcgta ccttctcaga gtcttcggtt tgggtctaac aatcttctag accctccttg 900
aaagatgggt ctctggagag ccaagataca gagaatgtcc cagttacact atcagaggag 960
aaccgttctg aaggaaaagt tggttttcag gcctataaga attacttcag agctggtgct 1020
cactggattg tcttcatttt ccttattctc gagcaccacc accaccacca ctga 1074

```

&lt;210&gt; 825

&lt;211&gt; 224

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 825

```

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5              10              15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20              25              30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35              40              45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50              55              60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65              70              75              80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85              90              95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100             105             110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115             120             125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Ile Arg Glu Lys Phe Ala
      130             135             140
His Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp

```

307

```

145          150          155          160
Ser Asp Lys Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp
          165          170          175
Glu Pro Tyr Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met
          180          185          190
Val Gln Gln Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala
          195          200          205
Lys Gln Arg Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
          210          215          220

```

&lt;210&gt; 826

&lt;211&gt; 357

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 826

```

Met Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg Arg
          5          10          15
Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg Gln
          20          25          30
Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr Ala
          35          40          45
Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser Phe
          50          55          60
Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly Ala
          65          70          75          80
Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro Ser
          85          90          95
His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln Gln
          100          105          110
Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly Lys
          115          120          125
Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala Leu
          130          135          140
Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile Gly
145          150          155          160
Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn Leu
          165          170          175
Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp Pro
          180          185          190
Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu Cys
          195          200          205
Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His Gln
          210          215          220
Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp Gly
225          230          235          240
Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly Ile
          245          250          255
Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln Pro
          260          265          270
Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu Ser
          275          280          285
Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly Ala
          290          295          300
Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu Glu
305          310          315          320
Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr Phe

```

308

325 330 335  
 Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Glu His  
 340 345 350  
 His His His His His  
 355

<210> 827  
 <211> 96  
 <212> PRT  
 <213> Homo sapiens

<400> 827  
 Met Gly Ile Arg Glu Lys Phe Ala His Cys Thr Val Leu Thr Ile Ala  
 5 10 15  
 His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys Ile Met Val Leu Asp  
 20 25 30  
 Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr Val Leu Leu Gln Asn  
 35 40 45  
 Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln Leu Gly Lys Ala Glu  
 50 55 60  
 Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg Trp Gly Phe Thr Met  
 65 70 75 80  
 Leu Ala Arg Leu Val Ser Asn Ser Leu Glu His His His His His His  
 85 90 95

<210> 828  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 828  
 cgcccatggg gatccgggag aaatttgccc actgc 35

<210> 829  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 829  
 cgccctcgagg gagtttgaga ccagcctggc caaca 35

<210> 830  
 <211> 38  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 830

309

gcatggacca tatgtcagcc attgagaggg tgtcagag 38

<210> 831  
 <211> 34  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 831  
 ccgctcgaga ataaggaaaa tgaagacaat ccag 34

<210> 832  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 832  
 gttgaattca tgacagggcc ccaggtg 27

<210> 833  
 <211> 30  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 833  
 cccctcgagt cactatggtc tgcctcttga 30

<210> 834  
 <211> 915  
 <212> DNA  
 <213> Homo sapiens

<400> 834  
 atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccagggtggg 60  
 cagggtattcg ccattccgat cgggcaggcg atggcgatcg cgggcagat caagcttccc 120  
 accgttcata tcgggcctac cgccttcctc ggcttggtg ttgtcgacaa caacggcaac 180  
 ggcgacagag tccaacgcgt ggtcgggagc gctcggcgcg caagtctcgg catctccacc 240  
 ggcgacgtga tcaccgcgt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300  
 gcgcttaacg ggcatcatcc cggtagcgtc atctcgttga cctggcaaac caagtccggc 360  
 ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catgcacggg 420  
 cccaggtgc tggcacgctg ctccgagtg gcttgtcctg ccttggtgc cacctctgcg 480  
 ggggtgcgtc tggagggggt ggaccggcca ccaaccttac ccagtcaagg aagtggatgg 540  
 ccatgttccc acagcctgag tggctgccac ctgatggctg atggagcaaa ggccttagga 600  
 aaagcagatg gcccttggtc ctacctttt gttagaagaa ctgatgttcc atgtcctgca 660  
 gcgagtgagg ttggtggctg tgccccagc tcctggcgcg ccctcgcaga ggtgactggt 720  
 tgctctttg gccctcttg ccttgcccag catgcacaag cctcagtgt actactgtgc 780



311

cgaagtcacg tggaggccag cctc

24

&lt;210&gt; 837

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 837

cctgaccgaa ttcattaact ggcctggac

29

&lt;210&gt; 838

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(166)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 838

Met	Gly	His	His	His	His	His	His	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg
1				5					10					15	
His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile
		20						25				30			
Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser
		35					40					45			
Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly
	50					55			60						
Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys	Val
65				70				75					80		
Asn	Val	Ser	Val	Val	Ser	Glu	Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro
			85					90					95		
Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Xaa	Gln	Xaa
			100				105					110			
Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr
		115				120					125				
Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly
	130					135				140					
Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu
145					150				155					160	
Lys	Thr	Val	Gln	Ala	Ser										
					165										

&lt;210&gt; 839

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(504)

&lt;223&gt; n = A,T,C or G

312

<400> 839  
 atggggccatc atcatcatca tcacgtggag gccagcctct ccgtacggca cccagagtac 60  
 aacagaccct tgctcgctaa cgacctcatg ctcatcaagt tggacgaatc cgtgtccgag 120  
 tctgacacca tccggagcat cagcattgct tcgcagtgcc ctaccgcggg gaactcttgc 180  
 ctcgtttctg gctggggtct gctggcgaac ggcagaatgc ctaccgtgct gcagtgcgtg 240  
 aacgtgtcgg tgggtgtctga ggaggtctgc agtaagctct atgaccgcgt gtaccacccc 300  
 agcatgttct gcgccggcgg agggcaanac cagaangact cctgcaacgg tgactctggg 360  
 gggcccctga tctgcaacgg gtacttgacg ggccttgtgt ctttcggaaa agccccgtgt 420  
 ggccaagtgt gcgtgccagg tgtctacacc aacctctgca aattcactga gtggatagag 480  
 aaaaccgtcc aggccagtta atga 504

<210> 840  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 840  
 ctcagggttc cggagccgcg g 21

<210> 841  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 841  
 ctatagaatt cattacaaaa aagctgggct ccagc 35

<210> 842  
 <211> 241  
 <212> PRT  
 <213> Homo sapiens

<400> 842  
 Met Gln His His His His His His Leu Arg Val Pro Glu Pro Arg Pro  
 1 5 10 15  
 Gly Glu Ala Lys Ala Glu Gly Ala Ala Pro Pro Thr Pro Ser Lys Pro  
 20 25 30  
 Leu Thr Ser Phe Leu Ile Gln Asp Ile Leu Arg Asp Gly Ala Gln Arg  
 35 40 45  
 Gln Gly Gly Arg Thr Ser Ser Gln Arg Gln Arg Asp Pro Glu Pro Glu  
 50 55 60  
 Pro Glu Pro Glu Pro Glu Gly Gly Arg Ser Arg Ala Gly Ala Gln Asn  
 65 70 75 80  
 Asp Gln Leu Ser Thr Gly Pro Arg Ala Ala Pro Glu Glu Ala Glu Thr  
 85 90 95  
 Leu Ala Glu Thr Glu Pro Glu Arg His Leu Gly Ser Tyr Leu Leu Asp  
 100 105 110  
 Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr Pro Lys  
 115 120 125

313

Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln Val Ile  
 130 135 140  
 Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala Pro Glu  
 145 150 155 160  
 Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln Val Lys  
 165 170 175  
 Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln Leu Ser  
 180 185 190  
 Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala Leu Lys  
 195 200 205  
 Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn Ser Tyr  
 210 215 220  
 Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro Ala Phe  
 225 230 235 240  
 Trp

&lt;210&gt; 843

&lt;211&gt; 729

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 843

atgcagcatc accaccatca ccacctcagg gttccggagc cgcgggcccg ggaggcgaaa	60
gcggaggggg ccgcgcgcgc gaccccgctc aagccgctca cgtccttcct catccaggac	120
atcctgcggg acggcgcgca gcggcaaggc ggccgcacga gcagccagag acagcgcgac	180
ccggagccgg agccagagcc agagccagag ggaggacgca gccgcgccgg ggcgcagAAC	240
gaccagctga gcaccggggcc ccgcgcgcgc ccggatgagg ccgagacgct ggcagagacc	300
gagccagaaa ggcacttggg gtcttatctg ttggactctg aaaacacttc aggcgccctt	360
cCaaggcttc cCaaacccc taagcagccg cagaagcgct cccgagctgc cttctcccac	420
actcaggtga tcgagttgga gaggaagtgc agccatcaga agtacctgtc ggcccctgaa	480
cgggcccacc tggccaagaa cctcaagctc acggagaccc aagtgaagat atggttcag	540
aacagacgct ataagactaa gcgaaagcag ctctcctcgg agctgggaga cttggagaag	600
cactcctttt tgccggccct gaaagaggag gccttctccc ggcctccct ggtctccgtg	660
tataacagct atccttacta cccatacctg cactgcgtgg gcagctggag cccagctttt	720
tggtaatga	729

&lt;210&gt; 844

&lt;211&gt; 27

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 844

ctactaagcg ctggagtgg ggtatcag

27

&lt;210&gt; 845

&lt;211&gt; 33

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer



314

<400> 845  
catcgagaat tcactactct ctgactagat gtc

33

<210> 846  
<211> 161  
<212> PRT  
<213> Homo sapiens

<400> 846  
Met Gln His His His His His His Ala Gly Val Arg Asp Gln Gly Gln  
1 5 10 15  
Gly Ala Arg Trp Pro His Thr Gly Lys Arg Gly Pro Leu Leu Gln Gly  
20 25 30  
Leu Thr Trp Ala Thr Gly Gly His Cys Phe Ser Ser Glu Glu Ser Gly  
35 40 45  
Ala Val Asp Gly Ala Gly Gln Lys Lys Asp Arg Ala Trp Leu Arg Cys  
50 55 60  
Pro Glu Ala Val Ala Gly Phe Pro Leu Gly Ser Asp Cys Arg Glu Gly  
65 70 75 80  
Gly Arg Gln Gly Cys Gly Gly Ser Asp Asp Glu Asp Asp Leu Gly Val  
85 90 95  
Ala Pro Gly Leu Ala Pro Ala Trp Ala Leu Thr Gln Pro Pro Ser Gln  
100 105 110  
Ser Pro Gly Pro Gln Ser Leu Pro Ser Thr Pro Ser Ser Ile Trp Pro  
115 120 125  
Gln Trp Val Ile Leu Ile Thr Glu Leu Thr Ile Pro Ser Pro Ala His  
130 135 140  
Gly Pro Pro Trp Leu Pro Asn Ala Leu Glu Arg Gly His Leu Val Arg  
145 150 155 160  
Glu

<210> 847  
<211> 489  
<212> DNA  
<213> Homo sapiens

<400> 847  
atgcagcatc accaccatca ccacgctgga gtgagggatc aggggcaggg cgcgagatgg 60  
cctcacacag ggaagagagg gccctcctg cagggcctca cctgggccac aggaggacac 120  
tgcttttctt ctgaggagtc aggagctgtg gatggtgctg gacagaagaa ggacagggcc 180  
tggtcagggt gtccagaggc tgctgctggc ttccctttgg gatcagactg cagggaggga 240  
gggcggcagg gttgtggggg gagtgcacgat gaggatgacc tgggggtggc tccaggcctt 300  
gccctgcctt gggccctcac ccagcctccc tcacagtctc ctggccctca gtctctcccc 360  
tccactccat cctccatctg gcctcagtgg gtcattctga tcaactgaact gaccataccc 420  
agccctgccc acggccctcc atggctcccc aatgccctgg agaggggaca tctagtcaga 480  
gagtagtga 489

<210> 848  
<211> 132  
<212> PRT  
<213> Homo sapiens

<400> 848  
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe

315

```

1           5           10           15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
                20           25           30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
                35           40           45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
                50           55           60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
                65           70           75           80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala
                85           90           95
Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser Val Asn Trp
                100          105          110
Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr Leu Ala Glu
                115          120          125
Gly Pro Pro Ala
                130

```

&lt;210&gt; 849

&lt;211&gt; 31

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 849

ggggaattca tcacctatgt gccgcctctg c

31

&lt;210&gt; 850

&lt;211&gt; 40

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 850

gggctcgagt cactcgccca cgaaatccgt gtaaaacagc

40

&lt;210&gt; 851

&lt;211&gt; 1203

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 851

```

atgcatcacc atcaccatca cagggccgcg tccgataact tccagctgtc ccagggtggg 60
cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120
accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180
ggcgacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
ggcgacgtga tcaccgcggt cgacggcgct cggatcaact cggccaccgc gatggcggac 300
gcgcttaacg ggcacatcc cggtgacgtc atctcgggtg cctggcaaac caagtccggc 360
ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catcacctat 420
gtgcgcctc tgctgctgga agtgggggta gaggagaagt tcatgaccat ggtgctgggc 480
attggtccag tgctgggcct ggtctgtgtc ccgctcctag gctcagccag tgaccactgg 540
cgtggacgct atggccgcgg ccggcccttc atctgggcac tgtccttggg catcctgctg 600

```

316

```

agcctctttc tcacccaag ggccggctgg ctagcagggc tgctgtgccc ggatcccagg 660
cccctggagc tggcactgct catcctgggc gtggggctgc tggacttctg tggccagggtg 720
tgcttcactc cactggaggc cctgtctctc gacctcttcc gggacccgga ccactgtcgc 780
caggcctact ctgtctatgc cticcatgac agtcttgggg gctgcctggg ctacctcctg 840
cctgccattg actgggacac cagtgccctg gccccctacc tgggcaccca ggaggagtgc 900
ctctttggcc tgctcaccct catcttcctc acctgcgtag cagccacact gctgtgtggct 960
gaggaggcag cgctgggccc caccgagcca gcagaagggc tgtcggcccc ctcttgtcgc 1020
ccccactgct gtccatgccg ggcccgttg gctttccgga acctgggcgc cctgcttccc 1080
cggctgcacc agctgtgctg ccgcatgccc cgcacctgc gccggctctt cgtggctgag 1140
ctgtgcagct ggatggcact catgaccttc acgctgtttt acacggattt cgtgggcgag 1200
tga 1203

```

&lt;210&gt; 852

&lt;211&gt; 400

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 852

```

Met His His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5      10      15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20      25      30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35      40      45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50      55      60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65      70      75      80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85      90      95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100      105      110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115      120      125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Ile Thr Tyr Val Pro Pro Leu
      130      135      140
Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr Met Val Leu Gly
      145      150      155      160
Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala
      165      170      175
Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp
      180      185      190
Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala
      195      200      205
Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
      210      215      220
Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val
      225      230      235      240
Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro
      245      250      255
Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu
      260      265      270
Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser
      275      280      285
Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu
      290      295      300
Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala
      305      310      315      320

```

317

Glu	Glu	Ala	Ala	Leu	Gly	Pro	Thr	Glu	Pro	Ala	Glu	Gly	Leu	Ser	Ala
			325						330					335	
Pro	Ser	Leu	Ser	Pro	His	Cys	Cys	Pro	Cys	Arg	Ala	Arg	Leu	Ala	Phe
			340						345				350		
Arg	Asn	Leu	Gly	Ala	Leu	Leu	Pro	Arg	Leu	His	Gln	Leu	Cys	Cys	Arg
		355					360					365			
Met	Pro	Arg	Thr	Leu	Arg	Arg	Leu	Phe	Val	Ala	Glu	Leu	Cys	Ser	Trp
	370					375					380				
Met	Ala	Leu	Met	Thr	Phe	Thr	Leu	Phe	Tyr	Thr	Asp	Phe	Val	Gly	Glu
385					390					395					400

```
<210> 853
<211> 20
<212> PRT
<213> Homo sapiens
```

```

<400> 853
Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
                    5              10              15
Ser Val Arg Val
          20

```

```
<210> 854
<211> 60
<212> DNA
<213> Homo sapiens
```

**<400> 854**  
ctgctccac ctccaccgc gctctgcggg gcctctgcct gtgatgtctc cgtacgtgtg 60

```
<210> 855
<211> 10
<212> PRT
<213> Homo sapiens
```

```
<400> 855
Ala Ser Ala Cys Asp Val Ser Val Arg Val
          5              10
```

```
<210> 856
<211> 30
<212> DNA
<213> Homo sapiens
```

<400> 856  
gcctctgcct gtgatgtctc cgtacgtgtg 30

```
<210> 857
<211> 9
<212> PRT
<213> Homo sapiens
```

<400> 857  
Ala Ser Ala Cys Asp Val Ser Val Arg  
1 5

<210> 858

318

<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 858  
Ser Ala Cys Asp Val Ser Val Arg Val  
5

<210> 859  
<211> 27  
<212> DNA  
<213> Homo sapiens

<400> 859  
tctgcctgtg atgtctecgt acgtgtg

27

<210> 860  
<211> 19  
<212> PRT  
<213> Homo sapiens

<400> 860  
Gly Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser  
5 10 15  
Ala Ser Asp

<210> 861  
<211> 19  
<212> PRT  
<213> Homo sapiens

<400> 861  
Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr  
5 10 15  
Met Val Leu

<210> 862  
<211> 19  
<212> PRT  
<213> Homo sapiens

<400> 862  
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala  
5 10 15  
Gln Leu Leu

<210> 863  
<211> 57  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(57)  
<223> n = A,T,C or G

<400> 863  
ggnathggnc cngtnytngg nytngtntgy gtnccnytny tnggnwsngc nwsngay 57

<210> 864  
<211> 57  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(57)  
<223> n = A,T,C or G

<400> 864  
gtncncncny tnytnytnga rgtnggngtn gargaraart tyatgacnat ggtnytn 57

<210> 865  
<211> 57  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(57)  
<223> n = A,T,C or G

<400> 865  
atggtncarm gnytntggt nwsnmgnytn ytnmgncaym gnaargcnca rytnytn 57

<210> 866  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 866  
Val Leu Gln Cys Val Asn Val Ser Val  
1 5

<210> 867  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 867  
Arg Met Pro Thr Val Leu Gln Cys Val  
1 5

<210> 868  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 868  
Asn Leu Cys Lys Phe Thr Glu Trp Ile  
1 5

320

&lt;210&gt; 869

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 869

Met Leu Ile Lys Leu Asp Glu Ser Val

1 5

&lt;210&gt; 870

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 870

Leu Leu Ala Asn Asp Leu Met Leu Ile

1 5

&lt;210&gt; 871

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 871

Leu Leu Ala Asn Gly Arg Met Pro Thr Val

1 5 10

&lt;210&gt; 872

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 872

Leu Met Leu Ile Lys Leu Asp Glu Ser Val

1 5 10

&lt;210&gt; 873

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 873

Val Leu Gln Cys Val Asn Val Ser Val Val

1 5 10

&lt;210&gt; 874

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 874

Gly Leu Leu Ala Asn Gly Arg Met Pro Thr

1 5 10

&lt;210&gt; 875

&lt;211&gt; 10

&lt;212&gt; PRT

321

&lt;213&gt; Homo sapiens

&lt;400&gt; 875

Thr Val Leu Gln Cys Val Asn Val Ser Val  
 1 5 10

&lt;210&gt; 876

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 876

Gly Val Leu Val His Pro Gln Trp Val  
 1 5

&lt;210&gt; 877

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 877

Val Leu Val His Pro Gln Trp Val Leu  
 1 5

&lt;210&gt; 878

&lt;211&gt; 1195

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 878

```

ccgagactca cgggtcaagct aaggcgaaga gtgggtggct gaagccatac tattttatag 60
aattaatgga aagcagaaaa gacatcacaa accaagaaga actttggaaa atgaagccta 120
ggagaaattht agaagaagac gattatttgc ataaggacac gggagagacc agcatgctaa 180
aaagacctgt gcttttgcac ttgcaccaa cagcccatgc tgatgaattt gactgccctt 240
cagaacttca gcacacacag gaactcttcc cacagtggca cttgccaatt aaaatagctg 300
ctattatagc atctctgact tttctttaca ctcttctgag ggaagtaatt caccctttag 360
caacttccca tcaacaatat ttttataaaa ttccaatcct ggtcatcaac aaagtcttgc 420
caatggtttc catcactctc ttggcattgg ttacctgcc aggtgtgata gcagcaattg 480
tccaacttca taatggaacc aagtataaga agtttccaca ttggttggat aagtggatgt 540
taacaagaaa gcagtttggg cttctcagtt tcttttttgc tgtactgcat gcaatttata 600
gtctgtctta cccaatgagg cgatcctaca gatacaagtt gctaaactgg gcatatcaac 660
aggtccaaca aaataaagaa gatgcctgga ttgagcatga tgtttggaga atggagattt 720
atgtgtctct gggaattgtg ggattggcaa tactggctct gttggctgtg acatctattc 780
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&lt;210&gt; 879

&lt;211&gt; 339

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



<210> 880

<211> 2172

<212> DNA

<213> Homo sapiens

<400> 880

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```

&lt;210&gt; 881

&lt;211&gt; 2455

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 881

```

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```

&lt;210&gt; 882

&lt;211&gt; 2455

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 882

```

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325

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```

&lt;210&gt; 883

&lt;211&gt; 62

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 883

```

Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
      5              10              15
His Gly Gly Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
      20              25              30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
      35              40              45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
      50              55              60

```

&lt;210&gt; 884

&lt;211&gt; 135

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 884

```

Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
      5              10              15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg
      20              25              30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
      35              40              45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
      50              55              60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
      65              70              75              80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
      85              90              95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
      100             105             110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
      115             120             125
Leu Leu Asn Tyr Gln Val Ser
      130             135

```

&lt;210&gt; 885

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 885

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln

```

326

```

          5          10          15
Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
          20          25          30
Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
          35          40          45
Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
          50          55          60
Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
          65          70          75

```

&lt;210&gt; 886

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 886

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

&lt;210&gt; 887

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 887

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

&lt;210&gt; 888

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 888

```

Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
          5          10          15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
          20          25          30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
          35          40          45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
          50          55          60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
          65          70          75

```

327

<210> 889  
 <211> 80  
 <212> PRT  
 <213> Homo sapiens

<400> 889  
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 Asn Lys Gln Ile Asn Lys Gln Thr Asn Lys Thr Glu Arg Phe Cys Cys  
                   20                  25                  30  
 Asn Val Gln Gly Ala Ile Cys Ser Phe Lys Lys Ile Ile Phe Gly Gln  
                   35                  40                  45  
 Ala Gln Trp Leu Thr Pro Val Ile Pro Ala Leu Trp Glu Ala Lys Val  
                   50                  55                  60  
 Gly Gly Ser Phe Glu Val Arg Ser Leu Arg Ser Ala Trp Pro Thr Trp  
                   65                  70                  75                  80

<210> 890  
 <211> 72  
 <212> PRT  
 <213> Homo sapiens

<400> 890  
 Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro His Asn Pro  
                   5                  10                  15  
 Ile Thr Ser His Gln Val Ser Ser Asp Thr Trp Asp Trp Val Gly Thr  
                   20                  25                  30  
 Gln Ser Gln Thr Val Ser Asp Ala Ala Gly Ala Gly Asp Thr Glu Thr  
                   35                  40                  45  
 Thr Gln Thr Trp Cys Leu Cys His Ser Ser Gly Leu Cys Leu Ser Pro  
                   50                  55                  60  
 Gly Pro Pro Ser Pro Ser Met Val  
                   65                  70

<210> 891  
 <211> 77  
 <212> PRT  
 <213> Homo sapiens

<400> 891  
 Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln  
                   5                  10                  15  
 Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His  
                   20                  25                  30  
 Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro  
                   35                  40                  45  
 Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln  
                   50                  55                  60  
 Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu  
                   65                  70                  75

<210> 892  
 <211> 60  
 <212> PRT  
 <213> Homo sapiens

<400> 892

```
<210> 893
<211> 76
<212> PRT
<213> Homo sapiens
```

<400> 893

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Met	Ser	Thr	Ser	Asp	Gly	Phe	Ala	Pro	Pro	Gln	Leu	Gly	Ser	Arg	
				20				25					30		
Cys	Ser	His	Ile	Arg	Gly	Pro	Ile	Lys	Ile	Ala	Arg	Asn	Lys	Phe	Pro
				35			40					45			
Arg	Thr	Leu	Thr	Ser	Gln	Glu	Leu	Arg	Arg	Phe	Ala	Glu	Tyr	Ser	Gly
				50			55				60				
Met	Met	Phe	Gly	Asp	Gln	Thr	Thr	Ala	Gly	Gln	Lys				
						70				75					

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<210> 894
<211> 2479
<212> DNA
<213> Homo sapiens
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<400> 894						
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ccgcaagggg tgatggccgg ctggttggtg gcactggcgg tcaattgtgg aaggaagagg 1800
gttggaggct gccccattg agatcttcct gctgagtcct ttccaggggc caattttgga 1860
tgagcatgga gctgtcactt ctgagctgct ggatgacttg agatgaaaaa ggagagacat 1920
ggaaggagg acagccaggt ggcacctgca gcggctgccc tctggggcca cttggtagt 1980
tccccagcct acttcacaag gggattttgc tgatgggttc ttagagcctt agcagccctg 2040
gatggtggcc agaaataaag ggaccagccc ttcattgggtg gtgacgtggt agtcacttgt 2100
aaggggaaca gaaacatttt tgttcttatg ggttgagaat atagacagt cccttggtgc 2160
gaggggaagca attgaaaagg aacttgccct gagcactcct ggtgcaggtc tccacctgca 2220
cattgggtgg ggctcctggg agggagactc agccttcttc ctcatcctcc ctgacctgc 2280
tcctagcacc ctggagagt aatgccctt ggtccctggc agggcgccaa gtttggcacc 2340
atgtcggcct cttcaggcct gatagtcatt ggaattgag gtccatgggg gaaatcaagg 2400
atgctcagtt taaggtacac tgtttccatg ttatgtttct acacattgat ggtggtgacc 2460
ctgagttcaa agccatctt 2475

```

&lt;210&gt; 895

&lt;211&gt; 492

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 895

```

Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
      5              10              15
Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20              25              30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35              40              45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50              55              60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65              70              75              80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85              90              95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100             105             110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115             120             125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130             135             140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145             150             155             160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165             170             175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180             185             190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195             200             205
Phe Met Lys Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys
      210             215             220
Leu Tyr His Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg
      225             230             235             240
Cys Leu Ala Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile
      245             250             255
Val Gly Gly Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser
      260             265             270
Leu His Val Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro

```





331

```

Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20      25      30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35      40      45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50      55      60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65      70      75      80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85      90      95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100     105     110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115     120     125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130     135     140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145     150     155     160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165     170     175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180     185     190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195     200     205
Phe

```

<210> 898  
 <211> 27  
 <212> PRT  
 <213> Homo sapiens

```

<400> 898
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
  1      5      10      15
Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg
      20      25

```

<210> 899  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

```

<400> 899
ggatccgccg ccaccatgtc actttctagc ctgct

```

35

<210> 900  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 900

332

gtcgactcag ctggaccaca gccgcag

27

&lt;210&gt; 901

&lt;211&gt; 34

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 901

ggatccgccg ccaccatggg ctgcaggctg ctct

34

&lt;210&gt; 902

&lt;211&gt; 27

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 902

gtcgactcag aaatcctttc tcttgac

27

&lt;210&gt; 903

&lt;211&gt; 936

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...()

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 903

```

atgggctgca ggctgntctg ctgtgcggtt ctctgtctcc tgggagcggc ccccatggaa 60
acgggagtta cgcagacacc aagacacctg gtcattggaa tgacaaataa gaagtctttg 120
aaatgtgaac aacatctggg tcataacgct atgtattggc acaagcaaag tgctaagaag 180
ccactggagc tcatgtttgt ctacagtctt gaagaacggg ttgaaaacaa cagtgtgcca 240
agtcgcttct cacctgaatg ccccaacagc tctcacttat tccttcacct acacacctg 300
cagccagaag actcggccct gtatctctgc gccagcagcc aagaccggac aagcagctcc 360
tacgagcagt acttcgggcc gggcaccagg ctacaggcca cagaggacct gaaaaacgtg 420
ttcccacccg aggtcgctgt gtttgagcca tcagaagcag agatctcca caccctaaag 480
gccacactgg tgtgcctggc cacaggcttc taccctgacc acgtggagct gagctggtg 540
gtgaatggga aggaggtgca cagtggggtc agcacagacc cgcagcccct caaggagcag 600
cccgcctca atgactccag atactgcctg agcagccgcc tgagggtctc ggccaccttc 660
tggcagaacc cccgcaacca cttccgctgt caagtccagt tctacgggct ctcgagaaat 720
gacgagtggg cccaggatag ggccaaacct gtcaccaga tcgtcagcgc cgaggcctgg 780
ggtagagcag actgtggctt cacctccgag tcttaccagc aaggggtcct gtctgccacc 840
atcctctatg agatcttgct aggggaaggcc acctgtgatg ccgtgctggt cagtgccctc 900
gtgctgatgg ccatggtcaa gagaaaggat ttctga 936

```

&lt;210&gt; 904

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

333

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...()

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 904

```

atgtcacttt ctacgtgct naaggtggtc acagcttcac tgtggctagg acctggcatt 60
gccagaaga taactcaaac ccaaccagga atgttcgtgc aggaaaagga ggctgtgact 120
ctggactgca catatgacac cagtgatcaa agttatggtc tcttctggta caagcagccc 180
agcagtgggg aaatgatttt tcttatttat caggggtctt atgacgagca aaatgcaaca 240
gaaggtcgct actcattgaa tttccagaag gcaagaaaat ccgccaacct tgatcatctcc 300
gcttcacaac tgggggactc agcaatgtat ttctgtgcaa tgagagaggg cgcgaggagga 360
ggaaacaaac tcaccttttg gacaggcact cagctaaaag tggactcaa tatccagaac 420
cctgaccttg ccgtgtacca gctgagagac tctaaatcca gtgacaagtc tgtctgccta 480
ttcaccgatt ttgattctca aacaaatgtg tcacaaagta aggattctga tgtgtatatc 540
acagacaaaa ctgtgctaga catgaggtct atggacttca agagcaacag tgctgtggcc 600
tggagcaaca aatctgactt tgcattgtga aacgccttca acaacagcat tattccagaa 660
gacaccttct tccccagccc agaaagttcc tgtgatgtca agctggctga gaaaagcttt 720
gaaacagata cgaacctaaa ctttcaaac ctgtcagtga ttgggttccg aatcctcctc 780
ctgaaagtgg ccgggtttta tctgctcatg acgtgcggc tgtggtccag ctga 834

```

&lt;210&gt; 905

&lt;211&gt; 311

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; variant

&lt;222&gt; (1)...(311)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 905

```

Met Gly Cys Arg Leu Xaa Cys Cys Ala Val Leu Cys Leu Leu Gly Ala
                    5              10              15
Val Pro Met Glu Thr Gly Val Thr Gln Thr Pro Arg His Leu Val Met
                20              25              30
Gly Met Thr Asn Lys Lys Ser Leu Lys Cys Glu Gln His Leu Gly His
                35              40              45
Asn Ala Met Tyr Trp Tyr Lys Gln Ser Ala Lys Lys Pro Leu Glu Leu
                50              55              60
Met Phe Val Tyr Ser Leu Glu Glu Arg Val Glu Asn Asn Ser Val Pro
                65              70              75              80
Ser Arg Phe Ser Pro Glu Cys Pro Asn Ser Ser His Leu Phe Leu His
                85              90              95
Leu His Thr Leu Gln Pro Glu Asp Ser Ala Leu Tyr Leu Cys Ala Ser
                100             105             110
Ser Gln Asp Arg Thr Ser Ser Ser Tyr Glu Gln Tyr Phe Gly Pro Gly
                115             120             125
Thr Arg Leu Thr Val Thr Glu Asp Leu Lys Asn Val Phe Pro Pro Glu
                130             135             140
Val Ala Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys
                145             150             155             160
Ala Thr Leu Val Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu
                165             170             175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr
                180             185             190
Asp Pro Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr
                195             200             205

```

334

Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro  
 210 215 220  
 Arg Asn His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn  
 225 230 235 240  
 Asp Glu Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser  
 245 250 255  
 Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr  
 260 265 270  
 Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly  
 275 280 285  
 Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala  
 290 295 300  
 Met Val Lys Arg Lys Asp Phe  
 305 310

<210> 906  
 <211> 277  
 <212> PRT  
 <213> Homo sapiens

<400> 906  
 Met Ser Leu Ser Ser Leu Leu Lys Val Val Thr Ala Ser Leu Trp Leu  
 5 10 15  
 Gly Pro Gly Ile Ala Gln Lys Ile Thr Gln Thr Gln Pro Gly Met Phe  
 20 25 30  
 Val Gln Glu Lys Glu Ala Val Thr Leu Asp Cys Thr Tyr Asp Thr Ser  
 35 40 45  
 Asp Gln Ser Tyr Gly Leu Phe Trp Tyr Lys Gln Pro Ser Ser Gly Glu  
 50 55 60  
 Met Ile Phe Leu Ile Tyr Gln Gly Ser Tyr Asp Glu Gln Asn Ala Thr  
 65 70 75 80  
 Glu Gly Arg Tyr Ser Leu Asn Phe Gln Lys Ala Arg Lys Ser Ala Asn  
 85 90 95  
 Leu Val Ile Ser Ala Ser Gln Leu Gly Asp Ser Ala Met Tyr Phe Cys  
 100 105 110  
 Ala Met Arg Glu Gly Ala Gly Gly Asn Lys Leu Thr Phe Gly Thr  
 115 120 125  
 Gly Thr Gln Leu Lys Val Glu Leu Asn Ile Gln Asn Pro Asp Pro Ala  
 130 135 140  
 Val Tyr Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu  
 145 150 155 160  
 Phe Thr Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser  
 165 170 175  
 Asp Val Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp  
 180 185 190  
 Phe Lys Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala  
 195 200 205  
 Cys Ala Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe  
 210 215 220  
 Pro Ser Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe  
 225 230 235 240  
 Glu Thr Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe  
 245 250 255  
 Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu  
 260 265 270  
 Arg Leu Trp Ser  
 275

335

<210> 907  
 <211> 1536  
 <212> DNA  
 <213> Homo sapiens

<400> 907  
 atgtacaacc tgttgctgtc ctacgacaga catggggacc acctgcagcc cctggacctc 60  
 gtgccaatc accagggctc caccctttc aagctggctg gaggaggagg taactactgtg 120  
 atgtttcagc acctgatgca gaagcggaag cacaccagc ggacgtatgg accactgacc 180  
 tcgactctct atgacctcac agagatcgac tcctcagggg atgagcagtc cctgctggaa 240  
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300  
 gagctggtga gcctcaagtg gaagcggtag gggcgccgt acttctgcat gctgggtgcc 360  
 atatatctgc tgtacatcat ctgcttcacc atgtgctgca tctaccgcc cctcaagccc 420  
 aggaccaata accgcacgag ccccgggac aacaccctct tacagcagaa gctacttcag 480  
 gaagcctaca tgaccctaa ggacgatata cggctggtcg gggagctggt gactgtcatt 540  
 ggggctatca tcatcctgct ggtagaggtt ccagacatct tcagaatggg ggtcactcgc 600  
 ttctttggac agaccatcct tgggggcccc ttccatgtcc tcatcatcac ctatgccttc 660  
 atggtgctgg tgaccatggt gatgcggctc atcagtcca gcggggagggt ggtacccatg 720  
 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagg attccagatg 780  
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840  
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900  
 gaggaccocg aggagctagg ccacttctac gactacccca tggccctggt cagcaccttc 960  
 gagctgttcc ttaccatcat cgatggcccc gccaaactaca acgtggacct gcccttcatt 1020  
 tacagcatca cctatgctgc ctttgccatc atcgccacac tgctcatgct caacctcctc 1080  
 attgccatga tgggcgacac tcactggcga gtggcccatg agcgggatga gctgtggagg 1140  
 gccagattg tggccaccac ggtgatgctg gagcggaagc tgctcgctg cctgtggcct 1200  
 cgctccggga tctcgagac ggagtatggc ctgggagacc gctggttcct gcgggtggaa 1260  
 gacaggcaag atctcaaccg gcagcggatc caacgctacg cacaggcctt ccacaccocg 1320  
 ggctctgagg atttggacaa agactcagtg gaaaaactag agctgggctg tcccttcagc 1380  
 cccacactgt cccttctat gccctcagtg tctcgaagta cctcccgag cagtggcaat 1440  
 tgggaaaagg ttcggaagg gaccctgagg agagacctgc gtgggataat caacagggtt 1500  
 ctggaggacg gggagagctg ggaatatcag atctga 1536

<210> 908  
 <211> 1533  
 <212> DNA  
 <213> Homo sapiens

<400> 908  
 atgtacaacc tgttgctgtc ctacgacaga catggggacc acctgcagcc cctggacctc 60  
 gtgccaatc accagggctc caccctttc aagctggctg gaggaggagg taactactgtg 120  
 atgtttcagc acctgatgca gaagcggaag cacaccagc ggacgtatgg accactgacc 180  
 tcgactctct atgacctcac agagatcgac tcctcagggg atgagcagtc cctgctggaa 240  
 cttatcatca ccaccaagaa gcgggaggct cgccagatcc tggaccagac gccggtgaag 300  
 gagctggtga gcctcaagtg gaagcggtag gggcgccgt acttctgcat gctgggtgcc 360  
 atatatctgc tgtacatcat ctgcttcacc atgtgctgca tctaccgcc cctcaagccc 420  
 aggaccaata accgcacgag ccccgggac aacaccctct tacagcagaa gctacttcag 480  
 gaagcctaca tgaccctaa ggacgatata cggctggtcg gggagctggt gactgtcatt 540  
 ggggctatca tcatcctgct ggtagaggtt ccagacatct tcagaatggg ggtcactcgc 600  
 ttctttggac agaccatcct tgggggcccc ttccatgtcc tcatcatcac ctatgccttc 660  
 atggtgctgg tgaccatggt gatgcggctc atcagtcca gcggggagggt ggtacccatg 720  
 tcctttgcac tcgtgctggg ctggtgcaac gtcattgtact tcgcccagg attccagatg 780  
 ctaggccctc tcaccatcat gattcagaag atgatttttg gcgacctgat gcgattctgc 840  
 tggctgatgg ctgtggtcat cctgggcttt gcttcagcct tctatatcat cttccagaca 900  
 gaggaccocg aggagctagg ccacttctac gactacccca tggccctggt cagcaccttc 960  
 gagctgttcc ttaccatcat cgatggcccc gccaaactaca acgtggacct gcccttcatt 1020  
 tacagcatca cctatgctgc ctttgccatc atcgccacac tgctcatgct caacctcctc 1080

336

```

attgccatga tgggcgacac tcaactggcga gtggcccatg agcgggatga gctgtggagg 1140
gccagattg tggccaccac ggtgatgctg gagcggaagc tgcctcgctg cctgtggcct 1200
cgctccggga tctgcggacg ggagtatggc ctgggagacc gctggttcct gcgggtggaa 1260
gacaggcaag atctcaaccg gcagcggatc caacgctacg cacaggcctt ccacaccgg 1320
ggctctgagg atttgacaa agactcagtg gaaaaactag agctgggctg tcccttcagc 1380
ccccacctgt cccttcctat gccctcagtg tctcgaagta cctcccgag cagtccaat 1440
tggaagagc ttcggaagg gaccctgagg agagacctgc gtgggataat caacaggggt 1500
ctggaggacg gggagagctg ggaatatcag atc 1533

```

&lt;210&gt; 909

&lt;211&gt; 511

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 909

```

Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
      5              10              15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
      20              25              30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
      35              40              45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
      50              55              60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
      65              70              75              80
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
      85              90              95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
      100             105             110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
      115             120             125
Phe Thr Met Cys Cys Ile Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn
      130             135             140
Arg Thr Ser Pro Arg Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln
      145             150             155             160
Glu Ala Tyr Met Thr Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu
      165             170             175
Val Thr Val Ile Gly Ala Ile Ile Ile Leu Leu Val Glu Val Pro Asp
      180             185             190
Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln Thr Ile Leu Gly
      195             200             205
Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe Met Val Leu Val
      210             215             220
Thr Met Val Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met
      225             230             235             240
Ser Phe Ala Leu Val Leu Gly Trp Cys Asn Val Met Tyr Phe Ala Arg
      245             250             255
Gly Phe Gln Met Leu Gly Pro Phe Thr Ile Met Ile Gln Lys Met Ile
      260             265             270
Phe Gly Asp Leu Met Arg Phe Cys Trp Leu Met Ala Val Val Ile Leu
      275             280             285
Gly Phe Ala Ser Ala Phe Tyr Ile Ile Phe Gln Thr Glu Asp Pro Glu
      290             295             300
Glu Leu Gly His Phe Tyr Asp Tyr Pro Met Ala Leu Phe Ser Thr Phe
      305             310             315             320
Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro Ala Asn Tyr Asn Val Asp
      325             330             335
Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala Ala Phe Ala Ile Ile Ala

```

337

```

          340          345          350
Thr Leu Leu Met Leu Asn Leu Leu Ile Ala Met Met Gly Asp Thr His
          355          360          365
Trp Arg Val Ala His Glu Arg Asp Glu Leu Trp Arg Ala Gln Ile Val
          370          375          380
Ala Thr Thr Val Met Leu Glu Arg Lys Leu Pro Arg Cys Leu Trp Pro
385          390          395          400
Arg Ser Gly Ile Cys Gly Arg Glu Tyr Gly Leu Gly Asp Arg Trp Phe
          405          410          415
Leu Arg Val Glu Asp Arg Gln Asp Leu Asn Arg Gln Arg Ile Gln Arg
          420          425          430
Tyr Ala Gln Ala Phe His Thr Arg Gly Ser Glu Asp Leu Asp Lys Asp
          435          440          445
Ser Val Glu Lys Leu Glu Leu Gly Cys Pro Phe Ser Pro His Leu Ser
          450          455          460
Leu Pro Met Pro Ser Val Ser Arg Ser Thr Ser Arg Ser Ser Ala Asn
465          470          475          480
Trp Glu Arg Leu Arg Gln Gly Thr Leu Arg Arg Asp Leu Arg Gly Ile
          485          490          495
Ile Asn Arg Gly Leu Glu Asp Gly Glu Ser Trp Glu Tyr Gln Ile
          500          505          510

```

&lt;210&gt; 910

&lt;211&gt; 134

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 910

```

Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
          5          10          15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
          20          25          30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
          35          40          45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
          50          55          60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
          65          70          75          80
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
          85          90          95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
          100          105          110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
          115          120          125
Phe Thr Met Cys Cys Ile
          130

```

&lt;210&gt; 911

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 911

```

Ala Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn Arg Thr Ser Pro Arg
          5          10          15
Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln Glu Ala Tyr Met Thr
          20          25          30
Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu Val Thr Val Ile Gly

```



338

35 40 45  
 Ala Ile Ile Ile Leu Leu Val  
 50 55  
  
 <210> 912  
 <211> 39  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 912  
 Glu Val Pro Asp Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln  
 5 10 15  
 Thr Ile Leu Gly Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe  
 20 25 30  
 Met Val Leu Val Thr Met Val  
 35  
  
 <210> 913  
 <211> 19  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 913  
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 <210> 914  
 <211> 52  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 914  
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 Tyr Ile Ile Phe  
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 <210> 915  
 <211> 213  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 915  
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 Ala Asn Tyr Asn Val Asp Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala  
 35 40 45  
 Ala Phe Ala Ile Ile Ala Thr Leu Leu Met Leu Asn Leu Leu Ile Ala  
 50 55 60  
 Met Met Gly Asp Thr His Trp Arg Val Ala His Glu Arg Asp Glu Leu

339

65		70		75		80									
Trp	Arg	Ala	Gln	Ile	Val	Ala	Thr	Thr	Val	Met	Leu	Glu	Arg	Lys	Leu
			85						90					95	
Pro	Arg	Cys	Leu	Trp	Pro	Arg	Ser	Gly	Ile	Cys	Gly	Arg	Glu	Tyr	Gly
		100						105					110		
Leu	Gly	Asp	Arg	Trp	Phe	Leu	Arg	Val	Glu	Asp	Arg	Gln	Asp	Leu	Asn
		115					120					125			
Arg	Gln	Arg	Ile	Gln	Arg	Tyr	Ala	Gln	Ala	Phe	His	Thr	Arg	Gly	Ser
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	145			150					155					160	
Phe	Ser	Pro	His	Leu	Ser	Leu	Pro	Met	Pro	Ser	Val	Ser	Arg	Ser	Thr
			165						170					175	
Ser	Arg	Ser	Ser	Ala	Asn	Trp	Glu	Arg	Leu	Arg	Gln	Gly	Thr	Leu	Arg
		180						185					190		
Arg	Asp	Leu	Arg	Gly	Ile	Ile	Asn	Arg	Gly	Leu	Glu	Asp	Gly	Glu	Ser
		195					200					205			
Trp	Glu	Tyr	Gln	Ile											
		210													

&lt;210&gt; 916

&lt;211&gt; 1302

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 916

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```

&lt;210&gt; 917

&lt;211&gt; 2061

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 917

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340

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&lt;210&gt; 918

&lt;211&gt; 957

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 918

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&lt;210&gt; 919

341

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 <212> DNA  
 <213> Homo sapiens

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<210> 920  
 <211> 318  
 <212> PRT  
 <213> Homo sapiens

<400> 920  
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                   20                  25                  30  
 Pro Leu Cys Ser Leu Tyr Leu Ile Ala Val Leu Gly Asn Leu Thr Ile  
                   35                  40                  45  
 Ile Tyr Ile Val Arg Thr Glu His Ser Leu His Glu Pro Met Tyr Ile  
                   50                  55                  60  
 Phe Leu Cys Met Leu Ser Gly Ile Asp Ile Leu Ile Ser Thr Ser Ser  
                   65                  70                  75                  80  
 Met Pro Lys Met Leu Ala Ile Phe Trp Phe Asn Ser Thr Thr Ile Gln  
                   85                  90                  95  
 Phe Asp Ala Cys Leu Leu Gln Met Phe Ala Ile His Ser Leu Ser Gly  
                   100                  105                  110  
 Met Glu Ser Thr Val Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala  
                   115                  120                  125  
 Ile Cys His Pro Leu Arg His Ala Thr Val Leu Thr Leu Pro Arg Val  
                   130                  135                  140  
 Thr Lys Ile Gly Val Ala Ala Val Val Arg Gly Ala Ala Leu Met Ala  
                   145                  150                  155                  160  
 Pro Leu Pro Val Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile  
                   165                  170                  175  
 Leu Ser His Ser Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys  
                   180                  185                  190  
 Asp Asp Ile Arg Val Asn Val Val Tyr Gly Leu Ile Val Ile Ile Ser  
                   195                  200                  205  
 Ala Ile Gly Leu Asp Ser Leu Leu Ile Ser Phe Ser Tyr Leu Leu Ile  
                   210                  215                  220  
 Leu Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys Ala Phe  
                   225                  230                  235                  240

342

Gly	Thr	Cys	Val	Ser	His	Val	Cys	Ala	Val	Phe	Ile	Phe	Tyr	Val	Pro
				245					250					255	
Phe	Ile	Gly	Leu	Ser	Met	Val	His	Arg	Phe	Ser	Lys	Arg	Arg	Asp	Ser
			260					265						270	
Pro	Leu	Pro	Val	Ile	Leu	Ala	Asn	Ile	Tyr	Leu	Leu	Val	Pro	Pro	Val
			275				280					285			
Leu	Asn	Pro	Ile	Val	Tyr	Gly	Val	Lys	Thr	Lys	Glu	Ile	Arg	Gln	Arg
			290			295					300				
Ile	Leu	Arg	Leu	Phe	His	Val	Ala	Thr	His	Ala	Ser	Glu	Pro		
305					310					315					

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<210> 921
<211> 28
<212> PRT
<213> Homo sapiens
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<400> 921
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          20                      25

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<210> 922
<211> 9
<212> PRT
<213> Homo sapiens
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<400> 922  
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5

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<210> 923
<211> 21
<212> PRT
<213> Homo sapiens
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<400> 923
Lys Met Leu Ala Ile Phe Trp Phe Asn Ser Thr Thr Ile Gln Phe Asp
                    5              10              15
Ala Cys Leu Leu Gln
                20

```

```
<210> 924
<211> 20
<212> PRT
<213> Homo sapiens
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```

<400> 924
Asp Arg Tyr Val Ala Ile Cys His Pro Leu Arg His Ala Thr Val Leu
                    5             10             15
Thr Leu Pro Arg
                20

```

```
<210> 925
<211> 37
<212> PRT
<213> Homo sapiens
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343

&lt;400&gt; 925

Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile Leu Ser His Ser  
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 Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys Asp Asp Ile Arg  
                   20                  25                  30  
 Val Asn Val Val Tyr  
                   35

&lt;210&gt; 926

&lt;211&gt; 13

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 926

Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys  
                   5                  10

&lt;210&gt; 927

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 927

Val His Arg Phe Ser Lys Arg Arg Asp Ser  
                   5                  10

&lt;210&gt; 928

&lt;211&gt; 22

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 928

Lys Thr Lys Glu Ile Arg Gln Arg Ile Leu Arg Leu Phe His Val Ala  
                   5                  10                  15

Thr His Ala Ser Glu Pro

20

&lt;210&gt; 929

&lt;211&gt; 3245

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 929

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gccgc

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&lt;210&gt; 930

&lt;211&gt; 1479

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 930

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ggcggggagg acgagaatcg gtgtgttcgc ctctacggat caaacttcat ccttcagggt 480

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tactcatctc agaggaagtc ctggcaccct gtgtgccaa acgactggaa cgagaactac 540
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gtggatgaca gcggatccac cagctttatg aaactgaaca caagtgccgg caatgtcgat 660
atctataaaa aactgtacca cagtgatgcc tgttcttcaa aagcagtggg ttctttacgc 720
tgtatagcct gcgggggtcaa cttgaactca agccgccaga gcaggattgt gggcggcgag 780
agcgcgctcc cgggggcctg gccctggcag gtcagcctgc acgtccagaa cgtccacgtg 840
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cctcttaaca atccatggca ttggacggca tttgcgggga ttttgagaca atctttcatg 960
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accaagaaca atgacattgc gctgatgaag ctgcagaagc ctctgacttt caacgaccta 1080
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aaggtgcttc tcattgagac acagagatgc aacagcagat atgtctatga caacctgatc 1260
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tggggttctg gctgtgccaa agcttacaga ccaggagtgt acgggaatgt gatggtattc 1440
acggactgga tttatcgaca aatgagggca gacggctaa 1479

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&lt;210&gt; 931

&lt;211&gt; 1476

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 931

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atggctttga actcagggtc accaccagct attggacctt actatgaaaa ccatggatac 60
caaccggaaa accctatcc cgcacagccc actgtggtcc ccactgtcta cgagggtgat 120
ccggctcagt actaccgctc ccccggtgcc cagtacgccc cgagggtcct gacgcaggct 180
tccaaccctg tcgtctgcac gcagccaaa tccccatccg ggacagtgtg cacctcaaag 240
actaagaaag cactgtgcat caccttgacc ctggggacct tcctcgtggg agctgcgctg 300
gccgctggcc tactctggaa gttcatgggc agcaagtgtc ccaactctgg gatagagtgc 360
gactcctcag gtacctgcat caaccctct aactggtgtg atggcgtgtc aactgcccc 420
ggcggggagg acgagaatcg gtgtgttcgc ctctacggat caaaCttcat ccttcagggtg 480
tactcatctc agaggaagtc ctggcaccct gtgtgccaa acgactggaa cgagaactac 540
gggcgggcgg cctgcaggga catgggctat aagaataatt tttactctag ccaaggaata 600
gtggatgaca gcggatccac cagctttatg aaactgaaca caagtgccgg caatgtcgat 660
atctataaaa aactgtacca cagtgatgcc tgttcttcaa aagcagtggg ttctttacgc 720
tgtatagcct gcgggggtcaa cttgaactca agccgccaga gcaggattgt gggcggcgag 780
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acggactgga tttatcgaca aatgagggca gacggc 1476

```

&lt;210&gt; 932

&lt;211&gt; 492

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 932



Met	Ala	Leu	Asn	Ser	Gly	Ser	Pro	Pro	Ala	Ile	Gly	Pro	Tyr	Tyr	Glu
Asn	His	Gly	Tyr	Gln	Pro	Glu	Asn	Pro	Tyr	Pro	Ala	Gln	Pro	Thr	Val
Val	Pro	Thr	Val	Tyr	Glu	Val	His	Pro	Ala	Gln	Tyr	Tyr	Pro	Ser	Pro
Val	Pro	Gln	Tyr	Ala	Pro	Arg	Val	Leu	Thr	Gln	Ala	Ser	Asn	Pro	Val
Val	Cys	Thr	Gln	Pro	Lys	Ser	Pro	Ser	Gly	Thr	Val	Cys	Thr	Ser	Lys
Thr	Lys	Lys	Ala	Leu	Cys	Ile	Thr	Leu	Thr	Leu	Gly	Thr	Phe	Leu	Val
Gly	Ala	Ala	Leu	Ala	Ala	Gly	Leu	Leu	Trp	Lys	Phe	Met	Gly	Ser	Lys
Cys	Ser	Asn	Ser	Gly	Ile	Glu	Cys	Asp	Ser	Ser	Gly	Thr	Cys	Ile	Asn
Pro	Ser	Asn	Trp	Cys	Asp	Gly	Val	Ser	His	Cys	Pro	Gly	Gly	Glu	Asp
Glu	Asn	Arg	Cys	Val	Arg	Leu	Tyr	Gly	Ser	Asn	Phe	Ile	Leu	Gln	Val
Tyr	Ser	Ser	Gln	Arg	Lys	Ser	Trp	His	Pro	Val	Cys	Gln	Asp	Asp	Trp
Asn	Glu	Asn	Tyr	Gly	Arg	Ala	Ala	Cys	Arg	Asp	Met	Gly	Tyr	Lys	Asn
Asn	Phe	Tyr	Ser	Ser	Gln	Gly	Ile	Val	Asp	Asp	Ser	Gly	Ser	Thr	Ser
Phe	Met	Lys	Leu	Asn	Thr	Ser	Ala	Gly	Asn	Val	Asp	Ile	Tyr	Lys	Lys
Leu	Tyr	His	Ser	Asp	Ala	Cys	Ser	Ser	Lys	Ala	Val	Val	Ser	Leu	Arg
Cys	Ile	Ala	Cys	Gly	Val	Asn	Leu	Asn	Ser	Ser	Arg	Gln	Ser	Arg	Ile
Val	Gly	Gly	Glu	Ser	Ala	Leu	Pro	Gly	Ala	Trp	Pro	Trp	Gln	Val	Ser
Leu	His	Val	Gln	Asn	Val	His	Val	Cys	Gly	Gly	Ser	Ile	Ile	Thr	Pro
Glu	Trp	Ile	Val	Thr	Ala	Ala	His	Cys	Val	Glu	Lys	Pro	Leu	Asn	Asn
Pro	Trp	His	Trp	Thr	Ala	Phe	Ala	Gly	Ile	Leu	Arg	Gln	Ser	Phe	Met
Phe	Tyr	Gly	Ala	Gly	Tyr	Gln	Val	Glu	Lys	Val	Ile	Ser	His	Pro	Asn
Tyr	Asp	Ser	Lys	Thr	Lys	Asn	Asn	Asp	Ile	Ala	Leu	Met	Lys	Leu	Gln
Lys	Pro	Leu	Thr	Phe	Asn	Asp	Leu	Val	Lys	Pro	Val	Cys	Leu	Pro	Asn
Pro	Gly	Met	Met	Leu	Gln	Pro	Glu	Gln	Leu	Cys	Trp	Ile	Ser	Gly	Trp
Gly	Ala	Thr	Glu	Glu	Lys	Gly	Lys	Thr	Ser	Glu	Val	Leu	Asn	Ala	Ala
Lys	Val	Leu	Leu	Ile	Glu	Thr	Gln	Arg	Cys	Asn	Ser	Arg	Tyr	Val	Tyr
Asp	Asn	Leu	Ile	Thr	Pro	Ala	Met	Ile	Cys	Ala	Gly	Phe	Leu	Gln	Gly
Asn	Val	Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Thr	Ser
Lys	Asn	Asn	Ile	Trp	Trp	Leu	Ile	Gly	Asp	Thr	Ser	Trp	Gly	Ser	Gly

347

Cys Ala Lys Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe  
 465 470 475 480  
 Thr Asp Trp Ile Tyr Arg Gln Met Arg Ala Asp Gly  
 485 490

<210> 933  
 <211> 100  
 <212> PRT  
 <213> Homo sapiens

<400> 933  
 Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu  
 5 10 15  
 Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val  
 20 25 30  
 Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro  
 35 40 45  
 Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val  
 50 55 60  
 Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys  
 65 70 75 80  
 Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val  
 85 90 95  
 Gly Ala Ala Leu  
 100

<210> 934  
 <211> 393  
 <212> PRT  
 <213> Homo sapiens

<400> 934  
 Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys Cys Ser Asn  
 5 10 15  
 Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn Pro Ser Asn  
 20 25 30  
 Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp Glu Asn Arg  
 35 40 45  
 Cys Val Arg Leu Tyr Gly Ser Asn Phe Ile Leu Gln Val Tyr Ser Ser  
 50 55 60  
 Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp Asn Glu Asn  
 65 70 75 80  
 Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn Asn Phe Tyr  
 85 90 95  
 Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser Phe Met Lys  
 100 105 110  
 Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys Leu Tyr His  
 115 120 125  
 Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg Cys Ile Ala  
 130 135 140  
 Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile Val Gly Gly  
 145 150 155 160  
 Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser Leu His Val  
 165 170 175  
 Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro Glu Trp Ile  
 180 185 190

348

Val Thr Ala Ala His Cys Val Glu Lys Pro Leu Asn Asn Pro Trp His  
 195 200 205  
 Trp Thr Ala Phe Ala Gly Ile Leu Arg Gln Ser Phe Met Phe Tyr Gly  
 210 215 220  
 Ala Gly Tyr Gln Val Glu Lys Val Ile Ser His Pro Asn Tyr Asp Ser  
 225 230 235 240  
 Lys Thr Lys Asn Asn Asp Ile Ala Leu Met Lys Leu Gln Lys Pro Leu  
 245 250 255  
 Thr Phe Asn Asp Leu Val Lys Pro Val Cys Leu Pro Asn Pro Gly Met  
 260 265 270  
 Met Leu Gln Pro Glu Gln Leu Cys Trp Ile Ser Gly Trp Gly Ala Thr  
 275 280 285  
 Glu Glu Lys Gly Lys Thr Ser Glu Val Leu Asn Ala Ala Lys Val Leu  
 290 295 300  
 Leu Ile Glu Thr Gln Arg Cys Asn Ser Arg Tyr Val Tyr Asp Asn Leu  
 305 310 315 320  
 Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly Asn Val Asp  
 325 330 335  
 Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser Lys Asn Asn  
 340 345 350  
 Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly Cys Ala Lys  
 355 360 365  
 Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe Thr Asp Trp  
 370 375 380  
 Ile Tyr Arg Gln Met Arg Ala Asp Gly  
 385 390

<210> 935  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

<400> 935  
 gtgctgtggg agtccccgcg gc 22

<210> 936  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

<400> 936  
 cgtgaactcg agtcattaga ttaacctcgt ggacgc 36

<210> 937  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

349

<400> 937  
gtgctgtggg agtccccgcg gc

22

<210> 938  
<211> 1158  
<212> DNA  
<213> Homo sapiens

<400> 938  
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tggacacttt gcgagggttt ttgctggctg ctgctgctgc ccgtcatgct actcatcgta 120  
gcccgcgccg tgaagctcgc tgctttccct acctccttaa gtgactgcca aacgcccacc 180  
ggctggaatt gctctggtta tgatgacaga gaaaatgata tcttcctctg tgacaccaac 240  
acctgtaaat ttgatgggga atgtttaaga attggagaca ctgtgacttg cgtctgtcag 300  
ttcaagtga acaatgacta tgtgcctgtg tgtggctcca atggggagag ctaccagaat 360  
gagtgttacc tgcgacaggc tgcattgcaa cagcagagtg agatacttgt ggtgtcagaa 420  
ggatcatgtg ccacagatgc aggatcagga tctggagatg gagtccatga aggtctctga 480  
gaaactagtc aaaaggagac atccacctgt gatatttgcc agtttggtgc agaattgtac 540  
gaagatgccg aggatgtctg gtgtgtgtgt aatatgtact gttctcaaac caacttcaat 600  
cccctctgcg cttctgatgg gaaatcttat gataatgcat gccaaatcaa agaagcatcg 660  
tgtcagaaac aggagaaaat tgaagtcatt tctttgggtc gatgtcaaga taacacaact 720  
acaactacta agtctgaaga tgggcattat gcaagaacag attatgcaga gaatgctaac 780  
aaattagaag aaagtgcag agaacaccac atacctgtc cggaacatta caatggcttc 840  
tgcatgcatg ggaagtgtga gcattctatc aatatgcagg agccatcttg cagggtgtgat 900  
gctggttata ctggacaaca ctgtgaaaaa aaggactaca gtgttctata cgttgttccc 960  
ggtctgttac gatttcagta tgtcttaatc gcagctgtga ttggaacaat tcagatttgt 1020  
gtcatctgtg ttgtgttcct ctgcatcaca aggaaatgcc ccagaagcaa cagaattcac 1080  
agacagaagc aaaatacagg gcactacagt tcagacaata caacaagagc gtccacgagg 1140  
ttaatctaata gactcgag 1158

<210> 939  
<211> 1020  
<212> DNA  
<213> Homo sapiens

<400> 939  
atgcagcatc accaccatca ccacgactgc caaacgcccc ccggtctgga ttgctctggt 60  
tatgatgaca gagaaaatga tctcttcctc tgtgacacca acacctgtaa atttgatggg 120  
gaatgtttta gaattggaga cactgtgact tgcgtctgtc agttcaagtg caacaatgac 180  
tatgtgcctg tgtgtggctc caatggggag agctaccaga atgagtgtta cctgcgacag 240  
gctgcatgca aacagcagag tgagatactt gtggtgtcag aaggatcatg tgccacagat 300  
gcaggatcag gatctggaga tggagtccat gaaggctctg gagaaactag tcaaaaggag 360  
acatccacct gtgataattg ccagtttggg gcagaatgtg acgaagatgc cgaggatgtc 420  
tggtgtgtgt gtaatatgta ctgttctcaa accaaactca atccccctg cgcttctgat 480  
gggaaatctt atgataatgc atgccaaatc aaagaagcat cgtgtcagaa acaggagaaa 540  
attgaagtca tgtctttggg tcatgtgtaa gataacacaa ctacaactac taagtctgaa 600  
gatgggcatt atgcaagaac agattatgca gagaatgcta acaaattaga agaaagtgcc 660  
agagaacacc acataccttg tccggaacat tacaatggct tctgcatgca tgggaagtgt 720  
gagcattcta tcaatatgca ggagccatct tgcaggtgtg atgctgggta tactggacaa 780  
cactgtgaaa aaaaggacta cagtgttcta tacgttgttc ccggtcctgt acgatttcag 840  
tatgtcttaa tcgcagctgt gatttgaaca attcagattg ctgtcatctg tgtggtgtgc 900  
ctctgcatca caaggaaatg cccagaagc aacagaattc acagacagaa gcaaaatata 960  
gggcactaca gttcagacaa tacaacaaga gcgtccacga ggtaaatcta atgactcgag 1020

<210> 940  
<211> 336

350

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 940

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Met Gln His His His His His His Asp Cys Gln Thr Pro Thr Gly Trp
                    5                      10                      15
Asn Cys Ser Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp
                20                      25                      30
Thr Asn Thr Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr
                35                      40                      45
Val Thr Cys Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val
                50                      55                      60
Cys Gly Ser Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln
                65                      70                      75                      80
Ala Ala Cys Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser
                85                      90                      95
Cys Ala Thr Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly
                100                      105                      110
Ser Gly Glu Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln
                115                      120                      125
Phe Gly Ala Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys
                130                      135                      140
Asn Ile Asp Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp
                145                      150                      155                      160
Gly Lys Ser Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln
                165                      170                      175
Lys Gln Glu Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn
                180                      185                      190
Thr Thr Thr Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp
                195                      200                      205
Tyr Ala Glu Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His
                210                      215                      220
Ile Pro Cys Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys
                225                      230                      235                      240
Glu His Ser Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly
                245                      250                      255
Tyr Thr Gly Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val
                260                      265                      270
Val Pro Gly Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile
                275                      280                      285
Gly Thr Ile Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr
                290                      295                      300
Arg Lys Cys Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr
                305                      310                      315                      320
Gly His Tyr Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
                325                      330                      335

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&lt;210&gt; 941

&lt;211&gt; 381

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 941

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Met Gln His His His His His His Val Leu Trp Glu Ser Pro Arg Gln
                    5                      10                      15
Cys Ser Ser Trp Thr Leu Cys Glu Gly Phe Cys Trp Leu Leu Leu Leu
                20                      25                      30

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351

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Pro Val Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe
      35              40              45
Pro Thr Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser
      50              55              60
Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr
      65              70              75              80
Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys
      85              90              95
Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser
      100             105             110
Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys
      115             120             125
Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr
      130             135             140
Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu
      145             150             155             160
Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala
      165             170             175
Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp
      180             185             190
Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser
      195             200             205
Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu
      210             215             220
Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr
      225             230             235             240
Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu
      245             250             255
Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys
      260             265             270
Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser
      275             280             285
Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly
      290             295             300
Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly
      305             310             315             320
Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile
      325             330             335
Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys
      340             345             350
Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr
      355             360             365
Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
      370             375             380

```

&lt;210&gt; 942

&lt;211&gt; 45

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 942

ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaac

45

&lt;210&gt; 943

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 943

Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys	Val	Asn
				5					10					15